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THE NUCLEUS–PLASMA PROBLEM

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INTRODUCTION

INQUIRIES into the precise relationship between the nucleus and the cytoplasm have fallen into disfavor, and not without some justification. The topic has proved to belong to that type of scientific problem which rarely yields important generalizations. This is the type where two (or more) virtually inseparable and difficultly controllable variables coexist, and where only one reacts neutrally to our measuring devices, yielding data interpretable quantitatively when neglecting the other. In such cases, the tendency is to ascribe all observed effects to the one easily measurable variable, and to disregard the other. Thus, since a very large body of pedigree culture data and of cytological observations are interpretable in terms of the grouping and the distribution of the genes, because these units ordinarily behave as if they form an isolated system unaffected by the cytoplasm, most geneticists have been led to assume that inheritance is completely under nuclear control and that the only remaining problem of heredity is the manner in which this control is exercised (see Morgan, 1927).

In taking this view of the nucleus-plasma problem, biologists have followed established precedent. It has been found in science that when a sub-universe of discourse can be disassociated from a larger universe and a means of studying behavior found which is but slightly affected by uncontrollable factors, the results usually

have high value in prediction. This is the reason for the extended progress of physics and chemistry. It is also the reason for the rapid progress in gene analysis. But, while chemists and physicists have tacitly agreed to neglect the problems arising when molecules or atoms are considered as wholes, the biologist can less easily evade the fact that his ideal goal is an understanding of the organism as an entity. He may never approach very close to this goal, but he must do what he can. For this reason, it seems fitting periodically to take stock of the knowledge bearing on the nucleus-plasma problem and to bring to light any new facts that may be pertinent, since this problem forms a very definite and important part of the problem of the organism as a whole. It is the more desirable because the subject remains debatable in the opinion of a number of competent workers.

Any acceptable discussion of this matter must, of course, be based upon the data obtained from the study of gene displacements and groupings considered as an isolated system. Here are included not only the effects of normal chromosome distributions, but also the effects of duplication, redundancy, deficiency, translocation, etc. Here is also incorporated the corroboratory evidence from cytology. In addition, one must keep in mind the known facts concerning the parental contributions of nuclear and of cytoplasmic constituents at fertilization, and the apparent behavior of these materials during the earlier stages of development. If this can be done, it is then convenient to consider the special evidence relative to the rôles of the nucleus and the cytoplasm under three heads: (1) the evidence from embryology; (2) the evidence from merogonous organisms; and (3) the evidence from reciprocal hybrids.

THE EVIDENCE FROM EMBRYOLOGY

The observations of the investigators working in experimental embryology frequently have been interpreted as favorable to the idea that the cytoplasm exerts a

genetic control over development that is independent of the nucleus; and this idea persists in various quarters. In brief, the situation is as follows: In all animal eggs there is a polarity, a symmetry, and a stratification of the cytoplasm, that are closely correlated with the early stages of embryonic differentiation and thus with the final stages of differentiation as represented by the adult. In other words, the early cleavage stages of the oösperm, while apparently allotting to each pair of daughter cells equivalent portions of chromatin, do not necessarily allot to the daughter cells equivalent amounts or equivalent types of cytoplasm. The cytoplasm in different parts of the oösperm exhibits differences in pigmentation, viscosity, and other properties, which may be followed visually during the early stages of cleavage. From such observations it appears that different types of cytoplasm exist and have an important influence during development. The cytoplasmic materials in the vicinity of the animal pole of the oösperm usually give rise to ectoderm, while those at the vegetative pole give rise to endoderm; the polar axis of the oösperm remains the polar axis of the blastula. In fact, the localization of cytoplasmic materials is so definite and so constant in the oösperm that characteristic patterns are recognizable for the different phyla; and seemingly identifiable portions of these patterns are traceable in the embryo after organ differentiation has occurred. In addition, there is much evidence to show that when the localization patterns of these fertilized eggs are disturbed experimentally, development exhibits correlated disturbances; and the situation is not changed if an unfertilized egg is stimulated to development by artificial means.

Such observations led Conklin (1915), following Boveri, to conclude that at the time of fertilization the hereditary potencies of the two germ cells are unequal, the early stages of development—including the polarity, symmetry, type of cleavage and the relative positions and proportions of future organs—being foreshadowed

in the cytoplasm of the egg cell and only the later differentiations being influenced by the sperm.

Loeb (1916) accepted this point of view and elaborated it still further. He proposed the hypothesis that all the generalized characteristics of the greater organic groups, down perhaps to those which differentiate genera, are determined by the maternal cytoplasm;[1] while simply the characteristics of species and varieties are controlled by the nuclei and determined by the chromosomes.

Loeb's hypothesis is not very satisfying as a scientific proposal. If true, the fact could not be demonstrated, since parental *differences* only can be detected and followed. If untrue, evidence for its falsity ordinarily could be obtained only indirectly, and with difficulty, by following the non-generalized differences between the greater taxonomic groups; and such crosses are rarely viable. Occasionally, however, a viable mutation occurs in a character that hitherto had been regarded as a trait common to a family or an order. The loss of the ligule in oats (Nilsson-Ehle, 1909), maize (Emerson, 1912), and rice (Katô, see Matsuura, 1933), is the best example from among several known in plants. No analogous instances have been so recognized in animals; but there seems to be no good reason why hornlessness in the Bovidae, taillessness in the Felidae, and numerous other similar cases, should not be regarded as acceptable examples. At all events, every such case known to-day has a Mendelian basis.

The idea of Boveri and Conklin is still less satisfactory as a working hypothesis from which to determine whether or not the cytoplasm serves as an independent vehicle of heredity; but it has aided us materially in discriminating between problems of inheritance and problems of development. There are no embryological facts incompatible with the supposition that the cytoplasm contains one or

[1] There is an interesting problem connected with this hypothesis. If species characteristics become generic during the course of evolution, there must be a shift in the control from the nucleus to the cytoplasm.

more reproducible substances of non-nuclear origin which carry hereditary potentialities to the next generation. There are no embryological facts incompatible with the assumption that the nucleus has complete control both of heredity and of development. One may interpret the situation by supposing that the nucleus is in charge of cytoplasmic differentiation, and that the developmental pattern is caused by the reactions thus made possible, when account is taken of cell succession and position.

There are, of course, various pieces of experimental work which are sometimes cited as arguments against this second view; but they are all susceptible of reasonable interpretations which are in harmony with the theory of nuclear control. Some of these cases have to do with a supposed maternal influence where enucleated eggs were fertilized with sperms from an animal belonging to a different species or genus (merogony). They will be considered later. Others are concerned with certain supposed hybrids in Echinodermata and Pisces, where no influence of the male was observable. These prove to be examples of induced parthenogenesis or induced apogamy. The parental nuclei may not fuse, as in many instances observed by Loeb, Kupelweiser and others. The sperm nucleus then degenerates, and the organism continues development either as a haploid or (after mitotic doubling) a diploid. More commonly, however, as numerous authors have shown, the chromatin of the sperm is eliminated after fusion of the parental nuclei has occurred, either immediately or during early cleavage stages. Occasionally no elimination of paternal chromatin is detectable, and the diploid progeny are still maternal in character. This is the case with certain crosses reported by Baltzer (1910) between various genera of sea urchins. Baltzer interpreted his results by assuming a latency or inactivation in the behavior of the paternal chromatin. It is more likely, however, as Ernst (1918) suggests, that a diploid egg developed (or per-

haps a haploid egg which doubled later) and that chromatin from the male was actually extruded without being detected.

It should also be mentioned that several cases are known where an excessive number of chromosomes contributed by one parent to a hybrid results in a kind of pseudo-dominance of that parent.

The embryological approach to the nucleus-plasma problem has also been of service by throwing into high relief the question of when genic activity is first exhibited. In some organisms, notably insects, an extraordinary amount of change occurs in the egg before fertilization. Here such nuclear control as exists must be wholly maternal, even though it be granted that the egg nucleus contains chromatin contributed by both parents of the previous generation. In addition, there are characteristics which appear after development of the oösperm begins that are attributable to the influence of the maternal constitution rather than to that of the oösperm. The determination of the point where parental control of the situation is superseded by filial control, so to speak, is important, therefore, both in the analysis of gene contributions and in estimating the influence of the cytoplasm.

There appears to be little, if any, activity shown by the genes of gametes. In an early paper, East and Park (1917, p. 604) concluded that the gametes of plants had a single function, the production of zygotes, and could not be expected to exhibit any differentiation traceable to their own genetic constitution. The data which led to this conclusion came from experiments on self-sterile plants which had been erroneously interpreted as showing only sporophytic influence. Nevertheless, the conclusion itself is probably not wholly incorrect. Later, Muller and Settles (1927) gave specific proof that the genes of Drosophila spermatozoa do not function before fertilization. It was based on critical evidence that there is no selective elimination of sperms having chromosome deficiencies that are lethal in the zygote. That

the conclusion may be generalized is made probable by the fact, unnoted by the authors, that the nucleus of the spermatozoön does not go into a true resting condition—a phenomenon probably prerequisite to the functioning of the genes. Muller and Settles thought, further, that their conclusion held for egg nuclei, though the evidence was less convincing. They felt, however, that the situation was different in plants on account of the complex gametophyte generation which has been developed in certain subdivisions.

There is, of course, no doubt about genic expression in gametophytes. In mosses, for example, meiotic divisions of sporophytic cells bring about segregation of the genes in the usual way, and subsequently numerous mendelizing characteristics are displayed during gametophytic development. Similarly, numerous instances of gametophytic expression due to gene activity are found in the pollen grains and the pollen tubes of the angiosperms, where only two cell divisions take place after meiosis. A full account of these examples is given in the monograph of Jones (1928) on selective fertilization. Some of the cases cited there may be due to reactions taking place in the sporophytic tissue of the pistil, but this is certainly not true in the majority of cases. Pollen tube factors have been located in definite linkage groups in maize (Mangelsdorf and Jones, 1926) and in Nicotiana (Brieger and Mangelsdorf, 1926), so there can be no doubt about specific gene control. And the facts of pollen tube growth, particularly those of self-sterile plants, require one to assume *mutual* reaction between pistil and pollen tube, and therefore an active expression of the genes in the pollen tube. On this point there is also a critical case in maize plants segregating for the pair of genes determining whether the reserve material shall be "waxy" or "starchy." Brink and MacGillivray (1924) showed that in such a plant 50 per cent. of the pollen grains actually carry the "waxy" material, and 50 per cent. carry the "starchy" material.

But in considering this series of facts, one should note that there is no evidence that the actual gametes which fuse to form the zygote exhibit genic activity. There is considerable evidence, in fact, that the male gametes of the higher plants are much like spermatozoa in having compressed nuclei with little cytoplasm, and that the eggs are like animal eggs in having enlarged resting nuclei with greater amounts of nucleoplasm and cytoplasm available. Even when there is but one cell division (or two) in the male gametophyte, there are manifest differences in the sister cells. The generative nucleus in the angiosperms is a flattish sharp-ended body set off in a small cell where little cytoplasm is available; the tube nucleus is a larger body, more nearly spherical, lying in a great quantity of cytoplasm. A consideration of these facts leads one to infer that there are essential differences in the male and the female gametes of plants which are very similar to those of the male and female gametes of animals, the most obvious ones being the stage in which the chromatin is found and the amount of cytoplasm available. Thus it seems probable that no genic activity takes place in the male gametes of either plants[2] or animals. The situation as regards the female gametes is still to be determined.

Gene activity in the zygote, on the other hand, is demonstrable at early stages of development, although examples are not numerous either in plants or in animals.

Legitimate citations from plants are: Color of the plumule sheath or coleoptile in Zea (Jenkins, 1925), and color of scutellum in Zea (Sprague, 1927); color of cotyledons in Glycine (Woodworth, 1921), Phaseolus (Tschermak, 1919), and Pisum (Mendel); and differences in the reserve materials of the embryo in Pisum (Mendel). There are also numerous cases of lethal genes and of genes affecting development of the endo-

[2] No waxy or starchy reserve materials have been demonstrated in the pollen grain cell containing the generative nucleus.

sperm; but it is a question whether such examples are acceptable.

The same remark may be made concerning the animal evidence. Hundreds of lethal genes are known which may prevent development entirely or may stop development at any stage. It seems hardly legitimate to cite as a sample of early genic expression cases where the machine does not operate at all; yet it also seems somewhat absurd not to cite cases where development is merely abnormal. What is one to say, for example, regarding such examples as the homozygous yellow mouse which at times shows failure to implant and at times goes through the first quarter of the prenatal life history; or the short-tailed lethal in mice which Chesley (1932) has shown to be detectable by a disturbance in the somites exhibited between the sixth and the eighth day after fertilization; or the "creeper" character in fowls (Landauer and Dunn, 1930) which puts in an appearance after thirty-six hours of incubation and kills 25 per cent. of the embryos after seventy-two hours? If these, and similar examples, are rejected, the earliest instances of genic expression that I have been able to discover are the appearance of blood groups in rabbits on the tenth day of embryonic life, and the appearance of iris pigmentation on the thirteenth day (both from Keeler, unpublished).

Morgan (1927) cites several larval characters in Lepidoptera; but, unfortunately, with the possible exception of the blood color differences in *Colias philodice* (Gerould, 1921), these gene manifestations come rather late in the life history. There is only one instance in Lepidoptera which, if confirmed, would be of primary importance in this connection. Tanaka (1924) interprets certain observations of Uda (1923) on inheritance of the color of the serosa in the silkworm as immediate expressions of gene activity. One race is characterized by slate-colored eggs, another by brown eggs. The two characters behave as if governed by a single pair of genes, slate being dominant. When the eggs of the

brown-colored race are fertilized by sperm from the slate-colored race, the color of the eggs changes shortly after the entrance of the sperm. Unfortunately, Uda's data are complicated by the presence of a second allelomorphic pair of genes; but one gets the idea, from Tanaka's statements, that he has made similar observations in cases where such complications were absent.

Clearly, the data on these matters are fragmentary. Nevertheless, sufficient evidence exists to warrant the conclusion that though the genes may possibly be dormant in the gametes, their activity is sometimes detectable at very early stages of zygotic development. That so little critical evidence has come to light is attributable in part to the neglect of the subject and in part to the scarcity of varietal differences discernible in early stages of embryonic life.

At the same time, one must not overlook the fact that a goodly number of embryonic character differences are not determined by the genetic constitution of the embryo, but rather by the genetic constitution of the mother. In the orderly diversification of ontogeny, a given change is dependent, to a marked extent, upon antecedent changes, one must agree; but one must also admit that this linear succession can not be charted accurately at present; therefore there is every reason to expect overlaps of various degrees. A late embryonic change may be particularly influenced by a change which immediately preceded it, or by a change which came very early. So, also, an early change may be brought about by slightly earlier manifestation of gene expression in the generation concerned, or may be influenced by the genetic constitution of the mother. Examples of such influence are common in silkworms and other Lepidopterans, though apparently much less common in the Diptera. A classical case is also found in snails, where direction of coiling of the shell, detectable at the first or second cleavage, is determined by the genetic constitution of the mother. Similar examples are found in plants. The inheritance

of pollen shape in Lathyrus (Bateson *et al.*, 1905) and of pollen color (from tapetum disintegration) in several species, may be cited.

The Evidence from Merogonous Organisms

It is difficult to imagine better evidence on the nucleus-plasma problem than that which would be derived from merogonous development, where an enucleated egg of one species is fertilized by the sperm of another species. Unfortunately, such evidence is difficult to obtain.

Boveri, between 1889 and 1918, carried out a number of experiments in which presumably enucleated eggs of one species of sea urchin were fertilized by sperm of another species. Development did not go beyond the pluteus stage; but among the plutei obtained, some were intermediate and some were paternal. He concluded that the first group were instances of hybridity and the second group instances of merogony. The natural conclusion was that the nucleus controlled affairs even in the cytoplasm of another species.

Seeliger (1894, 1896) and Morgan (1895) questioned this conclusion on the ground that there was no evidence to show that the members of the second group were not hybrids showing a kind of dominance of paternal characteristics. In his last paper, Boveri (1918) admitted the justice of this contention. Using improved technique, he had found that definitely enucleated eggs of Sphaerechinus, when fertilized with sperm of Echinus, did not develop beyond the early gastrula stage, and hence furnished no decisive evidence on the proposed question. Individuals which went further in development were shown by cytological investigation to be hybrids.

The other early investigations of this nature, of which there were a great number, may also be interpreted in this way or may be supposed to be examples of artificial parthenogenesis giving maternal characteristics only.

Spemann (1914) and Baltzer (1922) have constricted Triton eggs by means of ligatures, and have fertilized

both portions. Occasionally, merogonous development was obtained. The individuals were weak and dwarf, however, only one developing as far as metamorphosis. In no case could comparisons with the normal of the maternal and paternal species be made with any exactitude.

The same observation must be made regarding the experiments of Gunther Hertwig and Paula Hertwig (see Schleip, 1927, and Hertwig, 1927), who killed or inactivated the nuclei of the eggs of frogs and of Tritons by irradiation and then fertilized them with sperm of a different species. Some development was obtained, yet none of the individuals developed far enough, and in a sufficiently normal manner, to determine clearly whether they were matroclinic or patroclinic.

The botanical evidence is of a more decisive nature, though scanty. One should expect this to be true, since haploidy is a commoner and less disturbing phenomenon in plants than in animals. The surprising thing is that so few examples of merogony have been observed and studied.

Farmer and Williams (1898) and Winkler (1901) have described instances of merogony in a family of brown algae, the Fucaceae. Enucleated eggs fertilized with foreign gametes produced some poorly developed plants, from which one can hardly draw a more definite conclusion than to say that presumably the protoplasm of the mother had little or no influence.

The first good example of what must have been true merogony was observed by Collins and Kempton (1916). *Tripsacum dactyloides* was crossed with *Euchlaena mexicana*. One plant developed from Tripsacum seed which resembled the male parent exclusively. No cytological observations were made, but the breeding behavior indicated that it was a diploid.

The next case was described by Fruwirth (1923). Fruwirth had noted that when plots of *Vicia sativa* L. and of *Lens esculenta* Mönch. were contiguous, plants of Vicia sometimes developed from seeds of Lens. One

such plant he examined carefully. It was a normal Vicia plant except that it had flatter seeds than usual. This plant produced seven daughter plants which were all true to the Vicia specific characters. Fruwirth remarks, however, that they deviated somewhat from the Vicia varieties of the region. The blossoming period was slightly earlier, the flowers a little darker, and the seeds a little flatter—all of which was reminiscent of Lens. The color of the hilum, he states, was like Lens, while the color of the seeds departed noticeably from both Lens and Vicia. The last statement leads one to believe that perhaps Fruwirth did a bit of wishful thinking in saying that the variations observed were in the direction of Lens.

Anatomical and cytological studies of some of these plants were made by Weese (see Bleier). I have not been able to obtain Weese's paper, but, according to Bleier (1928), his results were not clear. Bleier found that the plants had the chromosome complement of Vicia (12) and not the chromosome complement of Lens (14). He believes that the influence of Lens protoplasm is indiscernible.

In 1927, Nawaschin reported what he calls a case of merogony in Crepis, though he does not use the term in the original sense. *Crepis tectorum,* a species from the sub-genus *Eucrepis* possessing four pairs of chromosomes, was crossed with pollen from *Crepis alpina,* a species from the sub-genus *Anisoderis* having five pairs of chromosomes. This hybrid, fertilized with pollen from *C. alpina,* produced three plants. One had chromosomes from *C. tectorum* exclusively, as shown by cytological examination; one had a combination of chromosomes from *C. tectorum* and *C. parviflora,* indicating a case of vicinism; and one had chromosomes exclusively from *C. alpina.* Nawaschin interprets the results by assuming that all gametes with mixed chromosomes die. If this interpretation be accepted, and it is undoubtedly the simplest, all one could argue from the case is that the cytoplasm formed under the influence of both species did

not influence the development of pure *alpina* characteristics.

The best example of merogony thus far reported was described by Kostoff (1929). Since Kostoff was working at this laboratory when he made his observations, I can corroborate his statements and add certain points from my own study of the case.

A triploid plant of *Nicotiana Tabacum,* having 72 chromosomes, was pollinated with pollen from *N. Langsdorffii,* where the diploid number of chromosomes is 18. These two species are widely separated taxonomically, differing markedly in habit, leaf, and flower. Comes (1899) places them in different sections of the genus. A large number of seeds and seedlings were produced, nearly all of which were probably hybrids, since they died after a few days. One plant, only, came to maturity. It had the 9 chromosomes of the size and form characteristic of *N. Langsdorffii.* The chromosome behavior has been described accurately by Kostoff. A most minute examination of the characters of this plant revealed absolutely no traces of the influence of the cytoplasm of the *N. Tabacum* plant upon which the seed grew. In every trait it was an example of *N. Langsdorffii,* though in size relations it was reduced to approximately three fourths of the measurements recorded for normal diploid plants of this species. It should be noted, however, that this reduction in size is probably to be expected in haploids of the group, for a haploid that I have obtained from normal stock had almost identical measurements.

Clausen and Goodspeed (1925) also mention a merogonous haploid which appeared after an attempt had been made to cross *Nicotiana glutinosa* with *N. Tabacum purpurea.* And Clausen and Lammerts (1929) describe a case which appeared when *N. digluta* (a synthetic amphidiploid species produced by crossing *N. Tabacum* and *N. glutinosa*) was mated with *N. Tabacum.* These writers also suggest that occasional pure plants of *N.*

sylvestris which are obtained in backcrosses of F_1 *sylvestris-Tabacum* × *sylvestris* are instances of diploid merogony. In none of these examples was any cytoplasmic influence detectable.

In addition to these instances, however, one should mention the important work of Harder (1927) on the Basidiomycetes *Schizophyllum commune* and *Pholiota mutabilis,* since these investigations are concerned with the production of merogonous forms of a particular type by the use of a novel methodology. When a plus mycelium from one of these species is allowed to conjugate with a minus mycelium from the other species, both the nucleus and the cytoplasm of the former pass into the conjugant cell of the latter. When this process is finished, the two nuclei lie side by side in the mixed cytoplasm for a time. Harder's contribution to technique was the removal of the maternal nucleus by means of a micromanipulator, thus allowing the male nucleus of one species to develop in the mixed cytoplasm of both species. Behavior could then be studied further by backcrossing with the species that furnished the male nucleus. Harder believed that although the results showed complete nuclear control of sexuality, nevertheless other characters showed a distinct influence of the cytoplasm.

(*To be continued*)

THE LIVING AND THE NON-LIVING[1]

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THE fundamental problem of general biology is the problem of the relation between the living and the non-living. In physical nature we meet with material and systems (unified collocations of matter and energy) of both kinds, although by far the larger part of nature is non-living in the biological sense of the term. The living we find experimentally to be dependent on the non-living in a definite manner; each living organism incorporates material and energy from its non-living environment, and after certain internal changes returns the material and the energy (at a lower potential) to the environment. The living organism thus represents a focal region to which matter and energy converge and from which later they diverge. In the interval they undergo chemical and physical transformations of a highly special kind with consequences which are expressed in the characteristic organization and activities of the organism. Typically this organization and this activity are of a kind "adapted" to promote the persistence of the species in its environment and are dependent primarily on chemical changes of a complex kind. We indicate the special importance of the internal chemical reactions when we speak of the organism as a metabolizing system. Metabolism, especially constructive metabolism, is the primary physical activity of life.

Regarded physically, the living organism represents a natural transformation-product of a definite kind. It comes into being and preserves stable existence only under conditions which, when we consider physical nature as a whole, are undoubtedly of a highly exceptional kind. The evidence from natural science is that life appeared

[1] Paper read before the Chaos Club, Chicago, December, 1932.

on the scene late in the evolutionary history of nature, and only in certain restricted localities where the environmental conditions, *e.g.*, of temperature and accessibility of chemically transformable substances, were especially favorable. The living system thus appears to science as an evolutionary derivative of the non-living: there was in past history a transition, sudden or gradual, from the non-living to the living. The evidence that living organisms may similarly originate "spontaneously" at the present time is inconclusive; but in any case each organism in the present is of necessity continually engaged in transforming non-living environmental materials and energy into its own living substance. This is the essential condition of its existence. We may say, then, that non-living nature is potentially living and requires only a certain rearrangement or reorganization of components in order to become living. The biological problem of organization has reference to the nature and conditions of this rearrangement.

Two chief questions arise at the outset. First, can we define clearly those general characters of nature which underlie and have rendered possible so remarkable a development? And, second, what are the essential distinguishing characters of the living, as contrasted with the non-living? Both questions are highly general and can be discussed without entering into biological detail. The first question relates to the general nature of the conditions required for any process of evolution; the second to the criteria of life as a special fact of nature. With regard to the second question, probably the fact of greatest general significance is that the living organism of which we know most, man himself, exhibits a double aspect. We know human beings not only objectively, *i.e.*, as physical systems performing complex evolutions in an external or public world, but also inwardly or subjectively, as individualized centers of experience from each of which the world is viewed in perspective. The world extends indefinitely in space and time outside of each

living and experiencing center. This central position determines the general aspect which nature presents to our observation. The general theory of relativity in physics now recognizes that the central status of the observer is always presupposed in the geometrical description of nature. This self-centeredness, or what may be called the psychological isolation or inwardness of each living organism, is a biological fact of the first importance which must be taken into account in every attempt at a comprehensive survey of the problem. Apparently it testifies to the special significance of internal as distinguished from external factors of determination in vital activity. In voluntary action, especially, initiation seems to come primarily from within, although external factors and restrictions, physiological and environmental, necessarily play their part in the total effect.

The problem of the place of life in nature may be considered from a purely scientific point of view, seeking inductively valid generalizations from known facts. A possible experimental side enters here: Can living matter be produced artificially in the laboratory from non-living matter? So far we have not succeeded in doing this, although we can synthesize biochemical compounds of all classes and can simulate by artificial models, often with surprising accuracy, many types of structure and activity formerly regarded as uniquely vital. Or the problem may be regarded as primarily a philosophical one, leading inevitably to metaphysical questions concerning the nature of existence itself, of which biological phenomena are one special manifestation. Our consideration in this paper will be mainly scientific, but by implication will have reference to the metaphysical problem also, since the problem of origins, *i.e.*, of diversification, is one that lies behind all problems of evolution.

Physical science assumes a nature or universe which is self-existent, *i.e.*, has a status independent of our apprehension. It regards the physical world as real and autonomous—as having an existence and activity of its own.

Our conceptions of it may be more or less adequate or serviceable, but at least the conception must not be confused with the natural reality as it is in itself. This reality is what it is—possesses its own being and characteristics—independently of mental representation, at least by the animal "mind." The autonomy of nature, it may be said, is usually accepted without question by scientific men.

In considering a problem such as the present, dealing with the transition from one kind of natural system to another, it is important that the most general characteristics of nature—and indeed of experience in general—should be held in mind as clearly as possible. We may assume that the evolution of the living began and came to its consummation in a world which already had certain definite characteristics or fixed properties—that is, features which are essential to natural existence as such and without which nature would not be nature. How can we define clearly these general features of natural existence?

Perhaps the most fundamental general fact relating to the structure of natural existence may be stated briefly thus: Nature shows everywhere a combination of constancy and change. It exhibits, first, a conservative side, consisting of constant elements, conditions or relations (invariants), and, second, a changing, novelty-producing or originative side (variants)—*i.e.*, one consisting of process as distinguished from static condition. Each of these appears integral to the other and presupposes the other. The two are interfused; apparently they represents parts of an indissociable unity; we distinguish them only by abstraction. Without conservation there can be no change; *i.e.*, certain constant or persistent conditions are required for the occurrence of any kind of event. The converse proposition is less evident; an unchanging existence seems conceivable; but at least we may say that without change (in the form of evolution) the constant conditions which we now find in physical nature could never have come into existence and established them-

selves Also it is to be noted that according to modern physics the most constant property of a physical entity, mass, is not a simply static or inert character, but is an active function or index of activity, *i.e.*, of energy. Experimentally mass appears associated with activity of a vibratory kind in the ultimate units, *i.e.*, with a regular and rapid periodicity of action or manifestation, as indicated by interference phenomena in protons and electrons. Physical evidence would thus indicate that without change, in the sense of activity, stations of constancy can be neither reached nor maintained; and this is especially true of living organisms. In this sense, change would appear necessary to the existence of constant conditions—so far, at least, as those have a physical side, *i.e.*, have the characters of natural reality. Change is also the substance of creativity. Whitehead's phrase, creativity is ultimate, expresses the fundamental status of creativity in nature. Creativity is the principle of novelty and lies behind evolution.[2]

The conditions just considered may be represented schematically thus:

Natural Reality

A. Conservative side: factors of stability (logical, including purely mathematical, relations; space-time; natural constants).

B. Originative side: factors of change (activity, will, creativity, emergence, evolution).

Following Whitehead, we may assume the conservative or stable conditions in nature to be partly innate or primordial, and partly derivative or consequent, *i.e.*, of evolutionary origin. The natural world, when observed without prepossession, seems always to present the general appearance of a permanent or stable substratum or background inside of which change occurs. We see this in every-day experience. When we look out on the natural scene, a landscape, familiar streets, the starry heavens, the attention can always distinguish these two

[2] *Cf.* A. N. Whitehead, "Process and Reality (Macmillan, 1929)," Chapter 2.

complementary aspects. We observe that much of nature, perhaps the greater part, is permanent, stable, unchanging; we receive this impression especially when we look at a distance. Another part, consisting especially of things close at hand and our own bodies, is continually active and changing. If we apply the microscope, we see that the smallest particles of matter are in a state of continual agitation, the Brownian movement. Scientific analysis, if pursued into finer detail, brings into evidence the kinetic agitation of molecules and atoms and indicates further that the ultimate physical units are fields of rhythmical or vibrational activity. Briefly, nature exhibits an unchanging background on the one side, combined with a continual undercurrent or inner process of change on the other.

The general features of the visual field are instructive. As a rule, most of the distinguishable objects in this field preserve their relative positions and the field itself has its constant characters, geometrical and other; but inside of it we observe changes; objects, or colored patches corresponding to objects, having themselves a certain permanency, shift their positions or change in size, shape, color or intensity. In other words, we perceive change always as occurring within a background or setting having a certain persistent identity or unchanging character. This combination of stability and change which we find in sense perception seems, so far as our experience indicates, to be a universal characteristic of natural existence. Everywhere nature, whether observed externally or felt as inner experience, presents this closely interknit combination of conservative elements with novel or changing elements.

Let us now consider briefly stability as a general fact or condition in nature, and its rôle in natural processes. First we note that stability and regularity are in essence one and the same, in the sense that regularity always implies the existence of some permanent or stable condition or conditions controlling the course of events. Thus the

regular alternation of day and night implies the stability of several underlying conditions which are physically uniform, *viz.*, the speed of rotation of the earth, its distance from the sun, the quantity of radiation received from the sun; given these constant factors, the result is a regularly recurring sequence or cycle of change. Now let us take a more complex case. The phonographic record of a symphony is highly complex; but the possibility of its regular reproduction on the instrument depends on a large number of factors of stability; some of those are: the shape and depth of the grooves cut in the disk, the special features of the mechanism for uniform rotation, the shape and pressure of the needle, the parts of the loud speaker; other extraneous factors are the constant properties of the atmosphere, the structure of the auditory apparatus, the nervous organization of the listener. Given these various factors of stability, *plus* a single factor of change, the uniform rotation of the disk, the whole cycle unfolds itself and may be repeated as often as desired. Similarly, to give a biological illustration, when we see the complexly organized human being developing with unfailing regularity from the egg —about forty to fifty million times each year—we come to realize the extraordinary stability of the vital process and of the structural and metabolic conditions that underlie its manifestations. What are the basic factors of stability in such a case? The answer, according to genetic theory, would be the genes; but it is evident that the stability of genes implies as its own basis a regularly repetitive and stable character in the process by which the genes are formed and reduplicated in each ontogeny. This process implies still further a stability in the chemical processes of specific metabolic synthesis, the fundamental vital activity. And this process presupposes many further factors of stability, having definite relation to special factors of change, as in the simpler illustrations just cited. Finally, a reference seems required to a stability which is ultimate and is necessary to any kind

of happening. It is especially important in considering our present problem, to recognize that a *process* or cycle, as well as a static character or condition, may have its own stability, in the sense of exactness of reduplication under definite conditions. Life, as a natural fact, is constituted by an integration of active processes as well as of static or structural conditions, the whole forming a complex system or organization which maintains and reproduces itself with regularity.

The illustrations just given are typical and may help us to realize clearly this general and fundamental condition pervading all natural existence. Stability, then, is basic and in physical nature is interwoven with change; the two form the warp and woof of the fabric. It even becomes evident, on further consideration, that without an underlying stability of conditions no progressive change of *any* kind would be possible. This is indicated with great appositeness by Whitehead in his "Process and Reality," where he quotes Milton's description of Chaos (p. 146):

> . . . . a dark
> Illimitable ocean, without bound,
> Without dimension, where length, breadth and heighth
> And time and place are lost; where eldest night
> And Chaos, ancestors of Nature, hold
> Eternal anarchy amidst the noise
> Of endless wars, and by confusion stand.

Note especially the phrase "and by confusion stand." In Chaos, the realm of confusion, conceived as utterly devoid of stability and order, there can be no progressive change of any kind. Where everything is in confusion things are necessarily static; no continued change in one direction would be possible under such conditions, since this would imply at least some stability—that of the space-time order. Hence, anything dependent on constancy in the cause-effect relation, such as progress, evolution, or development, would be impossible in Chaos. We are thus led irresistibly to the conclusion that a cer-

tain foundational element of order, constancy or stability is inherent or primordial in nature and forms the necessary condition for any kind of happening.

Certain unchanging factors or invariants are also present in all single natural events and form the indispensable prerequisite for the change itself, whatever its special character may be. Now the unchanging factor or invariant in any event, determining its special character, is what we call the scientific law of the event. An object drops from a table; the natural determining law is that of gravitation. If gravity were not persistent, the object would not fall. Hence the gravitational constant enters into the descriptive equation. We see, then, that in order to secure the conditions necessary for any example of change, and especially of complex change, certain factors must be constant, stable or invariant. These factors are represented in physical science by the constant terms and constant relations (algebraic signs, etc.) in the descriptive equation.

That nature has a certain permanent element of law-abidingness, constancy or stability has in a sense always been recognized. In Plato law and order are foundational; the forms of nature are permanent, and passing events are their transient manifestation. As a mathematician, Plato was deeply conscious of the omnipresence of formal conditions, independent of time or change. His predecessor, Heracleitus, was equally impressed with the *absence* of permanency in nature; but his saying, "All is flux," implies at least that the flux-like characteristic is a permanency. The modified Platonism of St. John's gospel—"In the beginning was the word" (Logos)—asserts again the primordial status of law and order.

Nevertheless, even to scientific men nature, and especially that part of nature consisting of living beings, does not appear as uniformly orderly or law-abiding. We have the philosophical question of how far the law-abiding element in nature extends, and how far nature has spontaneous or arbitrary elements or factors not entirely

fixed or predetermined in their operation. At various times in the history of science the view has prevailed that all events are determined completely and unequivocally by fixed conditions, *i.e.*, by factors already present and uniformly operative. This is essentially a "closed universe" conception, and as such absolutistic: reality as a whole is unchanging and only appears to us to change because of the accident of our situation as finite beings set inside the universe and viewing it in a partial manner.[3] Many scientific men are (or used to be) absolutistic in the sense of believing in a rigid or invariant causal interconnection between events. According to this view, there are never any alternative possibilities of outcome in any situation; each event presupposes all the others, both past and future; the whole system of physical reality is tightly interlocked. It seems clear, however, that this conclusion has been reached by formal deduction rather than by observation; and it does not seem consistent with what we know experimentally about physical nature at the present time. It would seem to be more in accordance with general as well as scientific experience to hold that in any natural occurrence both kinds of factors, (1) law-abiding and (2) spontaneous (*i.e.*, freely acting or physically indeterminate), are always present. The former determine the observed uniformity and regularity of natural events; the latter are responsible for a certain tendency to divergence from fixed rule and hence ultimately for the continual appearance of novelty in nature. These factors have a certain forward-tending quality and also a certain arbitrariness; they are responsible for that element in the future which is not unequivocally determined by the past. In the long run they determine the evolutionary trend. It is true that these factors always assert themselves under restrictions set by the actual state of nature at the particular place and time. The past is fixed and forms the necessary and inescapable condition of present action; but it is also to be

[3] F. Bradley's position, at least in his "Appearance and Reality."

noted that the conditions of natural action are not necessarily the same at all times. New rules are continually being made as new permanencies appear in nature. The essential point to be emphasized here is that the factors of the second class are to be regarded as only partly determinate in the usual physical or causal sense of the term. These factors, acting in the present, *i.e.*, in the transitional zone between the past (fixed) and the future ("not yet"), appear to have a certain range of indeterminacy, *i.e.*, alternative possibilities exist with respect to the precise time and direction of their incidence. Although this range may be small (being fixed for each electron event, according to Heisenberg's principle of indeterminacy, by the value of the quantum constant), it is sufficient to deprive natural events of the absolute invariance or fixity to which otherwise they would be held, and hence leaves room for a certain measure of spontaneity.

According to the view which I wish to present in this paper, the essential peculiarity of vital organization (as contrasted with the non-living part of nature) is that these spontaneous or originative factors are in living organisms enabled in some way to assert themselves in a unified and effective manner. An internal or individual determination, as distinguished from an external or mass determination, may thus under certain circumstances assume the upper hand and direct the course of vital events in a manner which is largely independent of external conditions. The spontaneity or innate variability of living organisms, as manifested, *e.g.*, in their genetic mutations, and especially in their individual behavior, is the most evident expression of these factors. As we shall indicate later, these factors appear to physical science ultimately as small-scale or intra-atomic factors.

Some further discussion of scientific procedure seems necessary at this point before coming back to the biological question. According to science, all things occur by rule, and it is the business of science first to determine

these rules and then to formulate them as clearly and definitely as possible. In this way we reach statements of broad or universal applicability which we call laws of nature. First it is to be noted that, in order to secure clearness, definiteness and unambiguity, we tend to frame such statements in a quantitative or numerical form. Hence the most concise form of scientific description is the equation. The situation represented by the terms and relations on one side of the equation is regarded as equivalent to—or determinative of—that represented on the other side.[4] The result is most satisfactory when the terms on one side are constant; the signs used indicate that these constants are interrelated in constant ways. Then we "understand" the conditions on the other side. We seek for an underlying invariance under which can be subsumed as great a variety of transformations as possible. The invariant factors and invariant relations represent the rules of the game—the restrictions under which the events occur. The generalizations of science are these rules. The analogy of games is worth examining. We note first that the rules, taken by themselves, do not determine how the game will turn out. There is always a certain unpredictability in the action of the players; this is what makes the game amusing. The players act according to rule, yet the outcome is uncertain. Some prediction is possible, but the detail can not be foreseen. We note also that a game is usually summarized by expressing the final results numerically, very much as in scientific description; the ball passes between the goal posts a certain number of times, a certain number of runs are hit, and so on. These facts alone are considered important in the statement of results at the end. The advantage of a numerical statement is that it gives an air of precision and is unambiguous. Every one knows (or thinks he knows) what it is to count; also when one number is greater than another. Measuring is

[4] Consider (*e.g.*) an equation such as the general statement of the gas laws, $PV = RT$.

similar to counting; we count the number of times a certain standard unit is contained in the measured object. Hence is derived the apparent definiteness of a quantitative description; the number assigned is a statement that something, *having itself constant properties,* is repeated in the system or situation a certain number of times with an additive or summational result, forming a definite totality. Closely related are the other scientific cases where the object or process under consideration conforms in its relations and character to geometrical diagrams, curves or formulae of different kinds. What is common to all these procedures is that definite and unambiguous formulation is sought. This aim is best secured by abstracting from the totality of the phenomenon the quantitative or relational aspects, since these are the aspects which are both universal and the most readily understood. The formulae thus derived represent rules which apply to an indefinitely large number of individual cases.

Natural science aims at representing phenomena by simple understandable terms, statements or formulae. Its ideal is to combine clearness, conciseness and unambiguity of statement with conformity to our experience of nature. And this procedure meets with remarkable success so long as it neglects or subordinates the individual complexity or particularity of things. This brings us to another point of general interest. Any single natural event or object when scrutinized closely appears complex; there is structure within structure, back to the electron which presumably has itself a structure not yet completely defined. But even the elements of the electron's structure would have their own structure, and so on. By the term structure we mean usually some kind of permanence of configuration, *i.e.,* constancy or stability in the character and interrelation of components. For purposes of scientific understanding we fix our attention not on the individual phenomenon with its indefinite complexity of detail, but on features (largely structural features) that are common to many individuals, *i.e.,* repeated or

general features. These are selected because they have a certain constancy, permanence or recurrence. They have the property of *lasting,* or of reappearing in time; of remaining themselves (self-identical) for a sufficient time so that they can be considered (at least provisionally) as constants. Then they can be "defined"; we can agree on a symbol or designation and treat them by quantitative methods.

In science, accordingly, the tendency is to neglect individual complexities as irrelevant and to focus attention on the broader, more regular and apparently simpler conditions. It should again be noted that anything, however complex, which is regular or recurrent or persistent, can be *conceived* simply; *i.e.,* a concept, picture, general image (with its appropriate label) can be formed of anything which is a fixture, or is repeated often enough to become a familiar object of experience. We have here exemplified the simplifying activity of the mind, its tendency to abstract, to summarize, to take short cuts, to synthesize. Evidently the possibility and validity of this procedure depend on the omnipresence of order, of a certain fundamental invariance or fixity underlying and conditioning the world of experience.[5] It is a fact that things happen in accordance with rule; uniformities do exist in nature; as we have seen, without such uniformities nothing could happen in a definite way; there could be no repetition, no classes with numerous similar individuals, no possibility of orderly evolution. Nature, supposing its existence to be at all possible under such conditions, would be chaotic. Science, therefore, is bound to insist on the all-importance of uniformity and regularity in nature.

This, however, is not enough. What is also to be noted is that uniformity in the method of happening, or law-abidingness, is always associated in nature with the existence of individual uniqueness in the single objects or events. This means that each event, considered as indi-

[5] The reference to the Kantian "categories" will be evident here.

vidual, always shows some departure from the strict letter of the rule. It is to this feature of reality that we must look if we are to understand in any way the diversification of nature, its extraordinary differentiation and variety, which reaches a climax in living things. As Newton points out in his "Scholium," uniformity taken by itself can not account for diversity. Uniformity is the necessary condition or prerequisite under which variety comes into being; but in order to account for the appearance and the special character of the variety it is necessary to refer to other and more special factors. Ultimately, it would seem, the reference is always to individual factors, *i.e.*, factors which have a certain autonomy or internal determination, independent of influences exerted from outside.

We come then to what may be called the problem of the diversification of nature; this is fundamentally the same as the problem of cosmology; and the problem of life has its evident relations to the problem of cosmology. In both cases the problem is one of origins, of creation, of emergence or evolution.

In great part this diversity of nature, as given to our observation or immediately experienced, appears not as original or primordial, but as a product of evolution. To scientific observation many complexities appear to emerge by degrees out of relative simplicity. This is the diversifying or evolutionary trend; one of its characteristics is that it leads from time to time to stations or conditions of at least relative stability; these may then serve as a new basis of departure for further evolution. Side by side with this diversifying trend, we observe another trend, apparently of a distinctly opposed kind. This is the tendency recognized and formulated in the second law of thermodynamics, according to which there is in nature a continual increase in the randomness of atomic motion, making for a progressive decrease of ordered condition or increase of entropy. When we consider this condition alone, the universe appears to be "running

down''; the differences of potential on which action depends are steadily decreasing. The world is steadily proceeding toward an ultimate balanced state, with potential uniformly diffused, the ''heat-death'' of Clausius.[6] And so we have the apparent paradox of the universe becoming more complex and diversified in its detail, as shown especially by life and its manifestations; while at the same time its element of randomness—of non-unified or non-progressive activity—continually increases. To scientific observation both tendencies appear actual. We find ourselves as parts of a universe in which a dissipative tendency, making for uniformity, coexists with a particularizing or individualizing tendency making for diversification.

Let us now consider more closely the steady conditions found in nature, those which remain unchanging (or virtually so) in time and so serve as a foundation on which change can proceed. These conditions include the various natural constants. Broadly we may classify natural factors as before into the two groups, (A) factors of stability, and (B) factors of change, the former serving as the foundation or prerequisite for the latter, as indicated in this somewhat more detailed scheme.

A. *Factors of Stability*: Invariants, Constants, ''Steady States,'' including:

(1) Formal Conditions (*primordial*). Geometrical (space-time) and formal conditions; subject-matter of pure mathematics and logic.

(2) Conservative Physical Conditions (*primordial?*) Conservation of energy, of mass, of number of electrons; fundamental natural constants such as velocity of light, quantum constant, electrostatic and gravitational constants, electronic charge.

(3) Stable Conditions Reached Historically (*consequent*). Fixed stations in evolution; atomic series; cosmography; geography; stable material structure or organization of any kind arising in evolution, including living organisms.

B. *Factors of Change*: Originative or Novelty-producing Factors; factors of evolutionary advance; ''free will''; autonomous or contingent factors, etc.

[6] This is the deduction from classical thermodynamics. Relativistic considerations may modify this conclusion: *cf.* the recent address of Professor R C. Tolman, ''Thermodynamics and Relativity,'' *Science*, 1933, Vol. 77, pp. 291 and 313.

The formal conditions are the subject-matter of logic and pure mathematics. The physical conditions represented by the laws of conservation are familiar; perpetual motion proves impracticable; dissipation of energy is seen in all large-scale physical events; we depend on friction in all our mechanisms; vibrations and rhythms are universal; any object put on the table rattles as it dissipates its energy in the familiar die-away manner; heat flows spontaneously from warm to cold and so on. Many of these effects are now physically interpreted as the statistical expression of molecular or atomic motions. The calculations of thermodynamics correspond remarkably well with the broader aspects of our experience of external nature; and the older ideas of rigid physical determinism received their chief support from this field. But here again we find that, although the statistical results are regular, the actions of the individual units, molecules, atoms and electrons always show a greater or less degree of non-predictability. This need not mean an absence of regularity in the behavior of units; the persistence and constant properties of atoms are sufficient evidence of their fundamental regularity of constitution and activity. It rather indicates that each atom possesses also a certain individual or inner determination or activity which is not (or only slightly) influenceable from outside. The internal or intra-atomic energy is enormously larger than the energy which is exchanged between atoms when they interact or when they receive or emit radiation. Apparently we must regard this internal energy as the source of the individual or unpredictable features in atomic behavior. It also appears as the source of energy transmitted through space in the form of radiation. The fact of atomism—*i.e.*, that nature acts as if it were an assemblage of discrete units, each being the seat of stable qualitative and quantitative characters, and also the focal point of a high concentration of energy—is perhaps the most significant of all the facts of physical nature. This discreteness of atoms, their abruptness

of demarcation or discontinuity, appears in marked contrast to the continuity of the conditions (space-time) in which they are set. A correlative fact is that the interchanges of energy in radiation or other physical action occur also in discrete units (quanta).

Our problem requires us to consider the atomistic constitution of nature in more detail. The basic natural entities or individuals appear to scientific observation as immensely numerous, extremely small on the space scale, and with some exceptions (the radio-active atoms) extremely durable in time or indestructible. They also show marked uniformity in their individual characters; experimentally all electrons are alike; the unit charge appears invariant.

This likeness makes it possible for any one atom (of a given species) or any one electron to be substituted for any other. In general, complete substitutability of elementary physical units seems to be the fundamental natural rule. Many steady conditions and many highly organized natural systems owe their characteristic features not to a static or unchanging balanced condition but to a continuous flow of atoms or electrons or energy. Certain components are being continually destroyed or eliminated from the system and are as continually being replaced by the formation or introduction of other units of the same *kind,* although individually different. So one soldier, in his quality as substitutable unit, may replace another in an army. This rule, which may be called the rule of the substitutability of units, is evidently indispensable to the production of any highly organized natural system, and has its most striking exemplification in living organisms, the substance of which is continually changing. Structural and other conditions which would not be possible in a system in static equilibrium are thus enabled to preserve a stable existence during the active life of the organism.

The atoms form a series, and in their physical constitution give evidence of an evolutionary origin. With electrons the case seems different. The electronic charge

appears constant and unchanging, although showing the two reciprocal or mutually complementary aspects, positive and negative. This contrast points to some primordial activity of a sundering or dichotomizing kind as the source of this primary physical diversification.[7] It should be emphasized that many, if not all, forms of large-scale natural action depend upon the equivalence of natural units. Their interchangeability evidently depends upon their similarity of *kind;* durability or constancy in the properties of the individual unit is also implied.

To illustrate the rôle played in natural processes by the stable products of evolution (A 3 in the scheme above), we may point to two examples, one simple, the other complex. The gravitational constant of the earth was determined in the past by the astronomical history of this planet. It has a nearly constant physical value for any latitude and enters as a factor into all terrestrial phenomena where weight plays a part. Similarly, the stability of the physiological conditions in any living organism, *e.g.*, a man, such as his average level of blood pressure or the properties of his nervous system, is reached historically in the individual development. The characteristic features of this individual development were established in the past during the evolutionary history of the species. Any feature of vital organization is only relatively stable; such stability as it has, however, forms the necessary condition or prerequisite for any dependent special activity exhibited by the organism. Thus the stable conditions established in a human being during his history (such as his moral character, special skill or knowledge, etc.) form the necessary foundation of his particular activity. The more complex this activity is, the more complex must be the underlying or conditioning constancy. We designate this constancy as his physical and mental constitution, and by biologists this is usually conceived as mechanism. This mechanism, however, is

[7] *Cf.* the discussion of "diadism" by C. S. Peirce: *Collected Papers,* Vol. 1 (Harvard University Press, 1931), paragraphs 430 and following.

to be regarded as only one condition of a man's special activity and not as in itself the final and complete determinant of that activity. What is especially to be noted at this point is that any complex activity necessarily requires as its condition an underlying stable foundation or organization which is correspondingly complex. The static complexity of the phonographic record in our former illustration furnishes an analogy. A constant complex mechanism may be actuated in an unlimited variety of ways, as we see (*e.g.*) in the playing of a musical instrument. The corollary follows that if the ultimate determination of a man's voluntary activity is (in the physical sense) intra-atomic, his large-scale physiological mechanism becomes not the primary determinant but merely the instrument or intermediary of that activity.

We thus reach the conclusion that while a certain basis of constancy is the necessary condition for any kind of definite action or process, this constancy does not determine by itself the character of the process in all its detail. It merely furnishes the stability of condition without which no event, simple or complex, could happen. A certain indeterminate residue, as yet incompletely conditioned, remains over. This residue is referred to the individuality or special uniqueness of the system or entity whose change constitutes the process in question. No two physical objects, no two actions are exactly alike; each has its individuality, asserts itself in its own peculiar way, dependent on its inner quality, constitution or impulse. This appears to be true even of atoms. It would seem, then, that the diversification of nature is ultimately to be referred to the internal character or individuality of the natural units. What has been called a contingent or casual or alogical element thus centers as a factor or ingredient in the basic natural entities.[8]

[8] For a critical philosophical discussion of the status of contingency in natural process, *cf.* the recent paper of Charles Hartshorne, "Contingency and the New Era in Metaphysics," *Jour. Philos.*, 1932, Vol. 29, pp. 421, 457.

Using the term casual or contingent does not carry us far in explanation; yet the fact pointed to is fundamental; this fact is the irreducibility of the single natural entity to any rigid rule or rules controlling *all* its manifestations. Its isolation exempts it (to that degree) from complete conformity to rule; *i.e.,* in the case of the single atom or electron, from complete control from the outside. Its determination becomes largely or mainly internal. We thus recognize a certain individualistic or self-determining character in the basic natural entities, although it is true that for most scientific purposes this individuality may be disregarded. In the elementary theory of probability "chance" deviations are usually regarded as equal in frequency in the different directions, so that their effect in the total process becomes negligible. But this procedure is merely in the interest of simplification. Actually we must ascribe to each atom a certain individuality of behavior, independent of influence exerted by other atoms; *i.e.,* one part of its determination is internal, the other external. To the fact of internal determination corresponds the large intra-atomic energy which vastly exceeds the energy exchanged in any single physical interaction. No one can predict exactly when the single radium atom will shoot off an electron, in spite of the fact that the statistical effects, as shown in the curve of radioactive decay, exhibit a high degree of regularity.

It is evident that a certain degree of isolation of the basic units is a necessary condition for this internal or individual determination. With a strict or complete interdependence of units no casual occurrence would be possible; thus a rigidly interlocked system would behave simply as a larger unit, and no spontaneous action of single components would be possible; the action of each elementary unit would be determined by the united influence of all the others. This is the condition which is (or was) assumed in the monistic or mechanistic world views. Incidentally, and quite logically, such views

denied the freedom of the will. The alternatives are clearly drawn; on the one side we have a strict interdependence of all the parts of nature—a monistic world view; on the other a partial interdependence of units, combined with a certain degree of autonomy or self-determination, which may be large or small according to circumstances, in the action of units. According to the second alternative, each unit possesses, as individual, a certain spontaneity, inner determination or "freedom," as a correlative of its isolation. This view may be classed as pluralistic; in philosophy the monadism of Leibnitz is the classical example.

To return from such strictly theoretical considerations to the immediate facts of experience, especially our experience of external nature, the physically given: what we observe is a diversified and changing world which yet is pervaded and conditioned by various underlying constancies or factors of stability. Physical analysis brings us by a combination of observation and abstract reasoning to the conception of an atomistically constituted world. This conception, however, assumes as existing at the outset a diversification of a certain kind. If we take any element of volume in nature, we have on the one hand "empty" space, on the other hand the various material objects, entities constituted of atoms, ultimately of electrons; at intervals pulses of radiant energy (quanta) are transferred from atom to atom. Atomism, then, would seem to be physically ultimate. Is there any way of accounting for the atomic constitution of nature?

While there is no physical solution of this problem at present, the monadism of Leibnitz furnishes a well-defined point of departure. According to the monadic theory, each element of the real, or monad, has a certain unchanging inner quality or stability corresponding to self-hood. Each real unit has its own inalienable quality and activity, is *different,* as individual, from others. Monads are conceived as isolated units actuated primarily from within. Leibnitz insists especially on the com-

plete insulation and autonomy of the monads—their "windowless" character. Although one monad may have certain characters in common with others—and indeed must have, in virtue of their common origin from one ultimate creativity—its main peculiarity is its special quality *of being itself,* which is not generic. Now the physical atom agrees with Leibnitz's conception in certain definite respects. Each atom persists in time, conserves its mass—*i.e.,* internal or self-contained energy—and properties (rule of conservation), and in most cases appears indestructible. Correlatively it retains its self-identity and excludes other atoms; *i.e.,* two atoms do not unite into a single atom of the same kind—impact is followed by deflection. Physical atoms, however, are not regarded as completely "windowless" or insulated from one another; they have a real interaction associated with interchange of quanta; *i.e.,* there is a mutual causal influence in the physical sense—not a "pre-established harmony." The essential point of agreement is that the physical as well as the metaphysical conception recognizes the individuality of each ultimate natural entity; and it places this individuality—and the obstinate retention of this individuality—at the basis of things.

Incidentally, we may note certain general physical consequences that follow from this persistence of the atomic individuality. Evidently there must be a limit to the convergence of material entities, but not to their divergence. In other words, indefinite expansion is possible for any atomically constituted system, but not indefinite contraction. Convergence brings into evidence the inveterate exclusiveness and particularity of each atomic unit. Each, as real existent, requires some space for the manifestation of its properties, *i.e.,* is not indefinitely compressible. Hence the general resultant of activity in any system isolated in space and consisting of atomic units interacting by impact or radiation would inevitably be either material expansion, or dissipation of radiant energy to the "empty" (non-resisting) surroundings.

The general thermodynamic law of dissipation (the second law) would seem to be an expression of this general condition. Whether this condition is also to be related to the astronomical evidence of a continual expansion of the physical universe[9] is a question of a somewhat related kind. Guye[10] quotes a reputed saying of Herodotus: "Given sufficient time everything possible will happen." Unlimited expansion appears physically possible in the universe as now constituted, but not unlimited contraction, and apparently we do have the physical evidence indicating expansion. In any case, limits must be assigned to the principle of the symmetry of time as recently advocated by G. N. Lewis[11] and others. The real universe appears to be hopelessly asymmetrical. Perfect symmetry can apply, it would seem, only to ideal constructions or models of restricted parts of nature, but not to nature as it exists and acts independently of scientific or other representation.

That a large part (at the very least) of atomic activity is of individual or internally determined character is indicated physically in a variety of ways. For example, we do not find that we can control experimentally (*i.e.*, by influences exerted from without) the detailed behavior of single atoms or electrons, *e.g.*, the time or direction of a quantum leap. Apparently the factors determining the exact conditions of any such transfer are mainly intra-atomic. A certain small fraction of the large store of intra-atomic energy becomes effective at certain times and in certain directions causing (*e.g.*) the emission of a quantum of radiant energy, or in a radium atom the emission of an electron. Since each such emission must have a definite direction in space and a definite instant of occurrence in time, we seem compelled to recognize the existence of intra-atomic directive factors controlling the

[9] *Cf.* A. S. Eddington's recent book, "The Expanding Universe" (Macmillan, 1933).

[10] C. E. Guye, "Physico-chemical Evolution" (Dutton's, New York, 1926), p 30.

[11] *Science*, 1930. Vol. 71, p. 569.

precise direction and time of the event. The nature of these factors can be only surmised, since they are physically or experimentally inaccessible at present.

The general scientific development which has led to the modern identification of matter (mass) and energy implies also that the chief energy of the cosmos is intra-atomic. This intra-atomic energy, however, is not entirely self-contained; atoms do influence one another; their isolation is not complete; evidently large-scale physical action depends on the unified action of large groups of atoms, *i.e.*, of material objects. Experiment shows that atoms interact by radiation; they have affinities for one another; they cohere with others of their own kind and of other kinds to form matter in mass with its infinite variety of compounds and structure. The transmitted energy of atoms, as exhibited in thermal, mechanical, radiant or electric effects, forms the condition of large-scale causation. It is always to be noted, however, that the ultimate source of this energy is intra-atomic. Without this intra-atomic energy, manifesting itself either as mass or as transmitted physical influence of various kinds, nature—in its present form at least—would have no real or substantial existence.

The problem of how energy came to be thus atomically subdivided and distributed in the cosmos is one for which there is no scientific solution at present. This physical state of things is one which we must simply accept, whether we regard it as primordial, or as a product of creative evolution—*i.e.*, as derivative or consequent.

The inference seems unavoidable that those special natural factors, which we may call vital factors (in contrast to non-vital factors), which have been chiefly responsible for the evolution of living organisms as a sharply distinct class of natural systems are, physically conceived, intra-atomic factors. The directive control so conspicuous in living organisms is to be referred to some feature or features of intra-atomic constitution, determining in some unknown way the direction and time of

quantum transfer. It is, of course, evident that large-scale causality of the type formulated in classical physics also plays its part in living organisms, which in many important aspects are large-scale systems. We find no evidence of the infringement of the general laws of energy in living organisms. But many of their most characteristic peculiarities, such as the progressive inner differentiation during ontogeny, the fine-grained character of nuclear and protoplasmic structure, the asymmetrical nature of many metabolic reactions, the spontaneity and selectivity of behavior in the organism as a whole, all point to the conclusion that their fundamental organization is different in kind from that of non-living systems. Our present hypothesis is simply that this organization is one in which the intra-atomic factors become important and individually effective in determining and directing the activities of the whole system. The characteristic vital (as distinguished from inorganic or non-vital) organization would then be one in which the intra-atomic forces are unified, directed and amplified in such a way as to produce a special and distinctive type of behavior, separating these organisms sharply from the great body of non-living systems in which the causation is chiefly of the large-scale or statistical type.[12]

The general laws of energy which determine the behavior of non-living material systems are now recognized as statistical in their nature; countless millions of atoms are concerned; their individual differences of activity are merged and have no importance in the behavior of the whole. In the living organism the conditions appear different. In higher animals especially, the responsive or neuromotor organization is in some instances so sensitive that a few quantum transfers or possibly even a single transfer may influence decisively the behavior of the whole organism. Apparently this is made possible through certain special types of conducting and amplify-

[12] *Cf.* my article, "The Directive Influence in Living Organisms," *Jour. Philos.*, 1932. Vol. 29, p. 477.

ing arrangement, depending on the special structure of the nervous system. The human retina approaches a condition of this kind in states of extreme sensitivity. The dark-adapted eye will respond to a very few quanta of radiation (or, according to some investigators, even to a single quantum) in the yellow region of the spectrum.[13] According to Einstein's principle of photochemical equivalence, this means initiation of response by chemical action confined initially to one or a few molecules. It implies further that physical influences originating in single atoms or groups of atoms (such as Eddington's key-atoms)[14] may control the whole large-scale activity of the organism. If we ask how it is physically possible that the transfer of one or a few quanta between certain atoms in a living cell may thus control the action of a large animal, we can only point to the characteristic irritability of the living protoplasm and its ability to transmit states of excitation over large areas. A slight local initiating disturbance may involve a stimulation which will activate an extensive physiological mechanism, very much as a spark may explode a barrel of gunpowder. The physical prerequisite for the regular production of such effects would be some combination or sequence of relay mechanisms, having general analogies to those used in electrical amplifying devices, but possessing also their own highly special structure and arrangement. In the structure of the physiological mechanisms subserving action in the higher animals (the nervous system with its correlative effectors) we can identify such relay and amplifying arrangements with a considerable degree of certainty. The retina has connections with an extensive neurone area in the occipital region of the cerebral cortex. This area has secondary connections with many other areas and tracts, including the motor tracts inner-

[13] This is the order of magnitude, although there is as yet no strict experimental proof that a single quantum is sufficient to excite visual sensation. For a recent study *cf.* P. Lecomte du Noüy, "Energy and Vision," *Jour. Gen. Physiol.*, 1921. Vol. 3, p. 743.

[14] *Cf.* A. S. Eddington, "The Nature of the Physical World," Chapter 14.

vating the voluntary musculature. The original stimulation involving only a few quanta of light is thus enabled to set in motion the whole complex mechanism.

In some such manner we may picture intra-atomic sources of initiation and control as expressing themselves in the activity of the whole large-scale organism. A purely physical model is thus presented of the sequence involved in the voluntary behavior of a human being. Evidently, in the case of any individual man, this activity manifests itself under restrictions imposed by his special large-scale and other structure and organization. As we have seen, stability of organization, *i.e.*, a mechanism, is required for any precise determination of activity. In its special nature such mechanism may be physical, chemical or physiological; a one-armed man can not play the violin; no more can a man deprived of his parathyroids or other sources of internal secretion necessary for muscular adjustment. But in the ultimate determining conditions of voluntary action there appears always to be something originative, not entirely determined by the past, pressing forward into the future and productive of novelty. This novelty-producing element requires a setting of stability in which to act. In any one person this setting is furnished by his existing organization, which has been partly established (in its main features) by past evolution and perpetuated by the hereditary mechanism, and partly altered in a special way ("conditioned") by individual experience.

We come again to our basic conception of the structure of natural reality as a combination of conservative and originative factors. The originative or "free" factors are to be regarded as the ultimate determinants of natural evolution—of cosmic evolution in its earlier stages, and finally of biological evolution. The presence of these factors explains why nature is not homogeneous or in a balanced state. They represent the ultimate creativity, which is active and individualizing in its character, although requiring a substratum of stability in which to

assert itself effectively. They would thus represent the ultimate source of diversity in the natural world. Their expression in evolution is gradual and progressive, because each advance requires first the establishment of a stable foundation. Hence also the course of nature, considered as a whole, is forward-tending and irreversible. In biological evolution the creative impulse has apparently found its culmination in man with his complex individual and social organization. Here again such stability as has been attained justifies itself only (or at least chiefly) as a basis for further advance; this advance requires creative activity of a kind making for further stability on a higher level. It should be noted, however, that a real and lasting stability, necessary for progress in any serious sense, presupposes the attainment of a sufficient degree of balance or harmony between the various interrelated components and activities. This does not seem in sight at present. Ethical, political and other implications enter here which are beyond the range of our present subject.

INDIVIDUAL VARIABILITY AND DIMORPHISM OF SOCIAL INSECTS

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INSECTS leading a social mode of life, and distinguished by the polymorphism of individuals, can be considered as an example, upon a large scale, of a natural experiment.

In this experiment the condition of nourishment is the agent calling forth the appearance of particular types of individuals, and influencing their variability.

There is no doubt that (in the course of their ontogeny) the nourishment of the worker individuals of the social hymenoptera may be looked upon as insufficient, in comparison with that of the fertile female.

As to the domestic bee, it is sufficiently known that the food of the larvae, out of which working bees will develop, is inferior to that of the larvae of queen bees, both quantitatively and qualitatively. In the bumble-bee the small size of the first spring workers and the gradual increase of the size of their bodies during summer, and likewise the sharper expression of the worker type, particularly in the small individuals, have been very exactly established in certain species by V. P. Derbeneff. For wasps it has long been known that the first workers are very small, that the size of the workers increases towards autumn, and that the workers developed out of the lower combs, which are the first the feeders meet with on returning with food, are of a larger size. The smallness of the first ant workers, when solitary females found new colonies, is well known; so is the more pronounced type of the worker in the small worker individuals, while the larger ones are sometimes nearer to the females in their structure. The minutest ant workers can also owe their small size to the presence of parasites, which deprive the growing larvae of their food. We have

more than once found particularly large worker ants with dilated abdomen and body rich in fatty matter, in the nests of *Formica pratensis,* in autumn; we have also found that the number of ovarial tubes in the workers of this species and in *Formica rufa* varies (in the same ovarium) from 2 to 6, and from 1 to 5 in *Camponotus herculeanus,* evidently in connection with the size of the body and the conditions of nutrition. Thus, insufficient nutrition of the larvae of worker individuals leads to a greater variability of the workers group in comparison with that of fertile females, exactly in the same way as in other animals and even plants, where, under the influence of unfavorable conditions of development, particularly of insufficient nutrition, a heightened variability has been ascertained many a time. Much lower coefficients of variability (and a less close correlative connection of characters) have been found by Derbeneff for the group of fertile females in bumble-bees, as compared to the workers; by Wright, Lee and Pearson in wasps, by Palenitshko in ants and by Warren in termites. This induces us to consider with extreme caution the supposition which takes the greater variability of the group of workers for a sign of its further differentiation.

In the experiment presented by nature, insufficient nutrition in the group of working individuals, differentiated from the group of fertile females both by the mean in the dimensions of their characters and by the degree of variability of the latter, carries out this differentiation apparently as completely as in a laboratory experiment. Even in those species where to the eye there seem to be transitional individuals, and where the character variability curves (drawn up on the basis of the measurements of the entire population of the nest, consisting of females as well as of workers) do not present bimodality, the application of the method of combined characters (Heincke) shows that there exists a transgression, and that any "transitional" individual can be placed with-

out any forcing in one of the groups. (*Agrobombus agrorum* Derbeneff.) The experiments of E. S. Smirnov and A. N. Thelochovtsev, on insufficient nutrition of the blow fly (*Calliphora erythrocephala*), have shown that the experimental series, when compared to the control series, present alterations in the forms of the connection between the characters; whence it results that no transitional forms are to be seen between the two series and that any individual can be placed in the one or in the other group according to the correlation of the characters it presents. In those cases where the group of working individuals progresses towards polymorphism in its evolution and becomes further differentiated into sub-groups, to judge by the researches of P. A. Novikov upon ants, the same process of separation into two groups repeats itself, and one group may be regarded as the experimental, and the other the control series. The small workers, as an experimental group, show a greater variability and a higher correlation of characters, in comparison with the group of large workers, which, in the given case, play the part of a control group. The only difference is that whereas the separation of the workers from the fertile females proceeds within the limits of the entire group of female individuals, that of the small workers from the large ones takes place within the group of working individuals. The observations of Derbeneff upon the degree of development of polymorphism in three species of bumble-bees (*agrorum, hortorum* and *lapidarius*), throws some light on the stages passed through in the course of the differentiation of the groups. It appears that the greater variability of workers and females coincides with a wide transgression between these groups, and that the further separation of both these groups and the formation of a hiatus between them coincides with a diminution of variability in each of the two groups taken separately; hence it follows that one can not, simply without any further cor-

roboration, consider the greater variability of a group as a sign of its incipient differentation. In *Agrobombus agrorum* the greater variability of the working individuals is, in reality a seasonal variability, depending as it does upon the gradual increase in the size of the body of the workers during the summer. On the contrary, the strong polymorphism of the ant, *Pheidole pallidula,* that manifests itself in the differentiation between the workers and the so-called soldiers, is accompanied, according to Novikov,[1] by an immense hiatus between workers and soldiers as well as by an excessively small variability of the two groups. Our comparison between the falling into groups with polymorphism and the results of the laboratory experiment can be pursued still further. Namely, cases of such variations during the experiments can be cited, where the series is either abbreviated or else does not appear at all owing to unfavorable conditions of nutrition. We were able to observe that in certain years fertile females do not appear at all in the nests of *Myrmica,* or develop in fewer numbers, or else do not develop in all the nests. In one such case, an exceedingly small number of females was found and those were dwarfed ones. The larvae which ought normally to develop into fertile females, in such cases produced working individuals, which thus, chronologically appeared before the males.[2]

The "control series" is also lacking in the young ant colonies founded by solitary females, and usually in artificial nests; on the other hand, the workers obtained in these cases are especially minute, with sharply pronounced worker's characters. In the latter cases there are neither females nor large workers ("control series" for the group of small workers).

[1] A work as yet unpublished.

[2] The first to hatch in the course of summer, in the *Myrmica,* are the young fertile females, then the males appear and lastly the young worker ants.

The study of variability connected with polymorphism, carried out upon a row of species, characteristic from this point of view and appropriately chosen, possessing either a highly developed polymorphism (ants, termites) or a feebly developed one (wasps, bumble-bees), will certainly make it possible in the future to trace the course of the development of polymorphism—a picture that will probably have also a wider general interest. Even now, one can outline, as yet in a great measure hypothetically, the stages according to which polymorphism develops in social *Hymenoptera.*

The first stage is that in which the group of investigated female individuals presents, in all the essential characters as regards polymorphism, variability curves approaching the normal one. Such a case it appears is realized in the *Ropalidiinae,* among the wasps, where there are fewer workers than females, and in *Vespa crabro* where, according to Janet (1895) the number of combs with large cells is greater than with small ones. In both these cases we have not so much a number of working individuals small in comparison with that of the females, as a number of sharply differentiated workers and females small when compared to the number of the transitional forms. Among the ants the given stage has been observed within the limits of the group of working individuals in those cases in which the workers are polymorphic to such a degree that their variability clearly surpasses the usual individual variation in those species where nevertheless they present a normal distribution of characters (for instance in *Formica exsecta* the coefficients of the variation of the most variable characters is about five per cent.). We expect that in all these cases there will be duly discovered a close transgression of the characters of females and workers, or of large and minute workers, thus creating the illusion of a homogenous material; in other terms, that we have here numerous transitional forms, constantly arising in

natural conditions with the greatest facility and even predominating numerically over either the one, or the other group separately.

The second stage is characterized by a certain flattening of the variation curves observed on the entire female population in the nest of certain bumble-bees (*agrorum*) and in the group of workers of certain ants (*Formica sanguinea.* C. about ten per cent.). The transgression established by Derbeneff in *agrorum* and which very probably exists in ants, is here far less considerable; transitional forms are constantly seen in nature, but in numbers they are far behind the group of workers (corresponding to small workers).

The third stage of the development of polymorphism, observed in the female individuals of *hortorum* among the bumble-bees, in the workers of *Camponotus herculeanus, maculatus* (C. more than 20 per cent.) and others among the ants, are characterized by a decrease of variability of the group of workers or of the small workers, the appearance of a bimodal curve, and a diminution of the number of transitional individuals, invariably found in natural conditions, but here inferior in numbers not only to the workers (corresponding to the small workers), but also to the females (corresponding to the large workers).

Lastly, the fourth and last stage is accompanied by a further restriction of variability in the group of workers (*lapidarius* among the bumble-bees), or that of small workers (*Pheidola pallidula* among ants; C. about five per cent. for the workers and for the soldiers taken separately), leading to the formation of a hiatus between the two groups; there are no "transitional" forms in nature as a norm, and experimentally they are either obtained with difficulty or not at all.

The evolutionary stages of polymorphism, thus traced out, show with sufficient clearness the connection of this phenomenon with individual variability. There is no

gradual transformation of individual variability into a polymorphic, as it might seem at first sight, on comparing the variability curves of species differing by their degree of polymorphism, but the latter takes its place. The existence of bimodality of different degrees in the curves does not prove the gradual appearance of dimorphism, which in reality is there from the very beginning, but only the degree of transgression existing in the polymorphous groups. This is already made evident by the fact that the behavior of diverse characters may be entirely different, and also by the fact that the moment when the existence of bimodality becomes apparent depends on the conditional peculiarities of the variation row. Individual variability could scarcely pass into polymorphic variability, were it only because it ought to be looked upon as a state and not as a process.

The character of many differences between dimorphous groups, being evidently one of adaptability and on the other hand, the independence from the chromosomic mechanism in the inheriting of these differences, have led to the notion that the reaction norm in social insects is of a peculiar character. Generally, one confines oneself to affirming that the capacity of developing, sometimes into one group, sometimes into another, lies within the bounds of the reaction norm in a given case.

D. M. Diakonoff (1926) has analyzed more closely the connection between dimorphism and the norm of reaction, and has proposed to designate this "a complicated reaction norm." If the character alters slowly, the environment values being low, then changes rapidly with the mean values and finally alters again slowly when they are high, the variation curve of the given character will show bimodality even should the conditions of environment change in a perfectly regular (equal) way, and the material studied should not present hereditary variations. It is this complicated interdependence between the dimension "environment" and the dimension

"character" that Diakonoff named "complicated reaction norm," and that he inclined to ascribe likewise to the polymorphic phenomena among social insects. However, the point of view we hold, as to the character of the correlations of polymorphic groups, that has already found its partial confirmation in existing facts, and according to which these groups are always distinctly separate and only present a greater or lesser degree of transgression, obliges one to go further and to admit that there are two (or more) reaction norms for every female individual of the social *Hymenoptera,* norms that are alternately realized.

That these two (or more) reaction norms coexist in one individual, can hardly be doubted, as there is no foundation for believing that the female eggs of social *Hymenoptera* are not similar; on the contrary, direct observations speak in favor of the identity of all the eggs of the female sex (*Apis mellifera*), joined to our own observations on ants showing that the larvae which ought to develop into a fertile female can give a worker ant. As for the question of an ontogenetical determination of the caste, it is far from being completely elucidated. If at present one can speak already with a certain assurance of the conditions of nutrition of the larvae, a further analysis of these conditions meets with considerable difficulties. Namely, there can exist here a possible influence of different modes of feeding the larvae and of the changes in the conditions of nutrition, which may depend upon the variations of the quantity of food in nature and upon the number of individuals, foragers, or feeders. Which of these two possibilities is the more probable one? The existence of two modes of feeding has been perfectly verified only in the domestic bee. In ordinary conditions no transitional forms are found between the queen and the working bee, and in experimental conditions these transitional forms can only be obtained with difficulty. When we subjected to hunger the larvae of ants destined to be females (*Camponotus, Myrmica*),

at different moments of their development, we never were able to obtain forms transitional between the queen ant and the worker, but either real fertile females, perhaps somewhat reduced in size, or else typical working individuals. Following particularly the fate of the ovaries, we did not meet a single case of a transitional ovary's being produced; at best it was possible to distinguish, in the rudiments of the ovaries which had taken the direction of developing into ovaries of workers, feeble signs of their transformation out of rudiments of ovaries of females. In nature, also, transitional forms between females and workers in ants represent frequently, by the structure of separate organs, either typical females or else workers. A *pterergate* of *Myrmica* we once chanced upon, presented with the general appearance of a worker, vestiges of broken, undeveloped anterior wings and the ovaries of a female.[3] The females of Lasius,[4] infested by round worms ("Mermis") which we investigated, had shortened wings at the same time with normally developed ovaries. The wings of all the individuals were in the same degree shortened in a very characteristic manner, being reduced to about the size of the wings of the males. If we recollect that the males, in most of the species of Lasius, are unusually minute by comparison with the females and that the myrmecologists for this reason consider that the females of *Lasius* have experienced an enlargement of the size of their body independently from the males, it will appear that in this case also the females respond to an infringement of normal nutrition, not in a haphazard, but in a perfectly definite manner, developing in the given case, not the characters of the worker individual (absence of wings), but a more ancient character of their own group.[5]

[3] With eight ovarial tubes in one and nine in the other.

[4] *L. niger* and *L. flavus*.

[5] According to M. N. Rimsky-Korsakof, the dwarf forms of aquatic *Prestwichia*, obtained in consequence of insufficient nutrition during the development of many larvae in one egg of the host, have shortened wings, but the degree of shortening is different.

The definite character of the reaction and the difficulty with which transitional forms seem to appear in ants, speak in favor of the opinion that in this group peculiar modes of feeding, if in general such really exist, can have but an auxiliary rôle, as compared to the capacity of reaction belonging to the organism itself. As to wasps and bumble-bees, one might think that the nutrition of the larvae changes according to the proportion existing between the number of feeders and that of the larvae fed during the summer, and that on the whole there are no peculiar modes of feeding. The females of bumble-bees are hatched towards autumn, when the proportion of the feeders to the fed favors their appearance, and when the workers can continue to be hatched simultaneously with the females only as an exception; therefore, the bumble-bee family, that has lost its female in spring, can not rear a new one, even if there were fecundated eggs, the necessary conditions of nourishment being lacking. In the middle intestine of larvae of *Vespa germanica* and *V. vulgaris,* as well of females as of workers, chitin remains of insects were found equally. In the first of the species named, the first large-sized comb cells destined for females can produce individuals intermediate between the females and workers, since, owing to the numerical proportion between the feeders and the fed, the females can not yet be hatched at the given time.

To conclude let us draw up our results. The so-called stases or castes of polymorphous social insects (fertile females — worker individuals; large workers — small workers; soldiers—small workers) are connected with each other as in a control and an experimental series in the laboratory experiment with insufficient nutrition. The experimental group (all the workers in relation to the females; the small workers in relation to the large ones or the small ones to the "soldiers") show a greater variability, greater (higher) correlative connections and alterations in the character connections; in consequence

of this last circumstance, the experimental group is in both cases completely distinct from the control group and can only show a greater or smaller transgression in relation to it. The transitional forms, which it would not be possible to refer to either of the two groups, are absent; each group has its own rĕaction norm, which does not constitute a part of a unique "complicated reaction norm."

The development of polymorphism, its evolution, is connected with a diminution of the variability of the groups (especially it seems of the "experimental" group), in consequence of which a hiatus appears, a break between the groups, which strikes one in the variability rows, or even at first sight. A high variability within a group cannot be simply considered as a sign of its more advanced differentiation.

In ontogenesis the determination of the group takes place under the influence of the conditions of nutrition of the larvae. The "experimental groups" feed below the optimum. The "control groups" can, in nature, fall out partially or entirely in conditions unfavorable for nourishment. The determining conditions of nourishment depend either upon the seasonal variation in the relations of the number of feeding individuals to that of those fed, or upon the existence of peculiar modes of feeding; the latter could develop directly out of the former, as with an abundance of feeders these last have sufficient time for a better preparation of the food; the first mode is more widely distributed. The separation (isolation) of the dimorphic group does not correspond to the separation of the conditions of nutrition; but it shows a capacity of reaction towards the gradual changes of the environment by means of two modes of development.

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A CHROMOSOMAL INTERCHANGE IN MAIZE INVOLVING THE ATTACHMENT TO THE NUCLEOLUS

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Chromosome No. 6 of maize is attached to the nucleolus near the end of the short arm, the attachment forming an enlarged reticulate region in the earlier prophase stages. Beyond this reticulate region is a satellite composed of four chromomeres. Burnham (1932) has reported an interchange in the satellite itself. Clarke and Anderson (1934) have reported a second case where the interchange is also in the satellite. A third case is under investigation by Mr. I. W. Clokey at this laboratory. The present case is one in which the interchange has taken place in the reticulate region, thus dividing the region of attachment to the nucleolus.

Source and Description

This interchange occurred following x-ray treatment in one of Dr. L. J. Stadler's cultures of maize at Columbia, Missouri. The plant was partially sterile. Dr. Stadler selfed it and sent the seed to the writer for further study. This was grown under culture No. 6470 and the interchanged chromosomes determined as No. 6 and No. 9 (Anderson and Clokey, 1934).

Cytological examination at pachytene showed the interchange within the reticulate region of chromosome 6 and about one third of the way out on the long arm of chromosome 9. A common reticulate region is formed by the normal chromosome 6 and the interchanged chromosomes. The chromosomes open out to form a ring at diakinesis. This is in contrast to the satellite interchanges (Burnham, 1932, Clarke and Anderson, 1934) where the satellite ends are not closely associated and

the interchange group forms an open chain of four chromosomes or breaks up into two "pairs."

The pollen sterility is also higher than in the satellite interchanges. Most of the plants would be classified as semisterile with about one half of the pollen visibly abnormal. In some cultures many of the plants show only about one fourth obviously bad pollen. In these plants, however, the normal appearing pollen grains differ markedly in size. Outcrosses using pollen from the heterozygous interchange plants give 50 per cent. normal and 50 per cent. partial sterile plants, showing that only the normal and interchange classes of pollen grains function. If either of the duplication-deficient classes of pollen function at all, it must be only rarely. The reciprocal outcrosses give similar results.

TABLE 1

PROGENY OF $\frac{C\ Sh\ Wx\ \mathsf{T}}{c\ sh\ wx\ +} \times c\ sh\ wx$

Crossover region	Constitution	Frequency		Total cross-overs	Per cent.	Standard
0	*C Sh Wx* T	77	168			
	c sh wx +	91				
1	*C sh wx* +	7	13	16	5.8	3.3
	c Sh Wx T	6				
2	*C Sh wx* +	33	59	66	24.0	20.3
	c sh Wx T	26				
3	*C Sh Wx* +	11	28	32	11.6	
	c sh wx T	17				
1, 2	*C sh Wx* T	1	3			
	c Sh wx +	2				
2, 3	*C Sh wx* T	2	4			
	c sh Wx +	2				

Like the other interchanges reported in maize, this one is viable in homozygous condition giving normal vigorous plants which are fully fertile.

Because of its interest in connection with the problem of the origin and function of the nucleolus a detailed

cytological study of this interchange has been made by Dr. Barbara McClintock. Her studies will be published in a cytological journal.

Linkage Relations with Chromosome 9

The interchange was crossed with a stock of *c sh wx*, and back-crossed to the same. Using **T** as a symbol for the interchange, the F_1 hybrid may be represented as *c sh wx*/**T**. The F_1 was used as female parent only. The data obtained are listed in Table 1.

The linear order is *c–sh–wx–***T** as expected, since the interchange is on the long arm of chromosome 9, not far from the point of interchange in semisterile–2 (Burnham, 1930), McClintock, 1930). The genes *c* and *sh* are known to be on the short arm (McClintock, 1931a, Creighton and McClintock, 1931), and *wx* is in the neighborhood of the spindle fiber insertion (unpublished data of Dr. C. R. Burnham).

The crossing-over in the two regions *c–sh* and *sh–wx* is somewhat above the amounts listed as standard in the Cornell mimeograph sheets of 1930. The deviation is about twice the probable error in both cases. No control data are available for the stocks used.

The crossing-over between *wx* and the point of interchange is 11.6 per cent.

Linkage Relations with Chromosome 6

The strain in which this interchange occurred had yellow endosperm and was recessive for the *Pl* factor for purple plant and anther color. Crosses were made with a white endosperm, purple anther plant (*y Pl*). The hybrids were crossed both ways with the multiple recessive. The data obtained are summarized in Table 2.

While the two reciprocal outcrosses differ in the amount of crossing-over, both place the order definitely as **T**–*y*–*Pl*. The gene *Pl* is known to be at about the middle of the long arm of chromosome 6 (McClintock, 1931b, Cooper and Brink, 1931, Brink and Cooper, 1932).

TABLE 2

PROGENY OF OUTCROSSES OF $\frac{T\,Y\,pl}{+\,y\,Pl}$ WITH THE MULTIPLE RECESSIVE

Region	Constitution	F_1 ♀ × recessive ♂			Recessive ♀ × F_1 ♂		
		Frequency	Total cross-overs	Per cent.	Frequency	Total cross-overs	Per cent.
0	T *Y pl*	62			72		
	+ *y Pl*	52			83		
1	T *y Pl*	1	7	4.9	19	45	17.3
	+ *Y pl*	4			19		
2	T *Y Pl*	11	23	16.2	24	67	25.8
	+ *y pl*	10			36		
1, 2	T *y pl*	1			2		
	+ *Y Pl*	1			5		
	Total	142			260		

The position of *y* in the chromosome is uncertain, but it is known to be in the direction of the satellite from *Pl* (McClintock, 1931b). Tests now under way indicate a position for *y* in the long arm about midway between the spindle fiber insertion and the position of *Pl*. The standard crossing-over value for the *y–Pl* region is 28.5 per cent. On the opposite side of *y*, there is only one definitely known gene, *po* (polymitotic). The crossing-over between polymitotic and yellow endosperm is 12 per cent. (Beadle, 1931). The position of *po* in the chromosome is unknown.

The data of Table 2 give about 5 per cent. of crossing-over between the interchange and *y* and 16 per cent. between *y* and *Pl*, where the F_1 was used as female parent in the outcross. In the reciprocal outcross, the corresponding values were 17 per cent. for the T–*y* region and 26 per cent. for the *y–Pl* region. Some of the recorded crossovers in the latter may be cases of heterofertilization (Sprague, 1932), but the frequency of such would not be expected to be above 1 or 2 per cent. The classification of yellow endosperm is sometimes difficult, but in the present case the separation was rather clear.

The inequality of the crossing-over values in the reciprocal outcrosses suggests extensive suppression of crossing-over in megasporogenesis as compared with microsporogenesis. At present we have no measure of crossing-over in the region between *y* and the reticulate region, but the long section of the chromosome involved suggests that for this region the interchange reduces crossing-over even in microsporogenesis.

Summary

In an x-rayed culture of maize, an interchange was found involving chromosomes 6 and 9.

The point of interchange was within the reticulate region of chromosome 6 and about one third the distance out on the long arm of chromosome 9.

Linkage data with *c, sh* and *wx* of chromosome 9 show the interchange to be beyond waxy with 11.6 per cent. of crossing-over in the *wx*–T interval.

Linkage data with *y* and *Pl* give the order as T–*y*–*Pl*. The per cent. of crossing-over differed in reciprocal crosses.

as female	T–*y* = 4.9	*y*–*Pl* = 16.2
as male	T–*y* = 17.3	*y*–*Pl* = 25.8

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STUDIES ON REVERSE MUTATIONS IN *DROSOPHILA MELANOGASTER*

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INTRODUCTION

SINCE it first became known that hereditary changes could occur through mutation, perhaps no discovery has had more significance from the point of view of evolution than the fact that the phenomenon of mutation was reversible. Reverse mutations have shown that, at least in some cases, no irreparable loss or alteration has occurred in the genetic constitution of the organism after mutation, but rather a change which might, at some time, revert to its original condition. However, and notwithstanding the importance of this subject, our knowledge concerning it has been rather fragmentary and incomplete. Accordingly, it has been the purpose of the experiments described in this paper to extend our understanding of reverse mutations using *Drosophila melanogaster* as a subject for study.

The distribution of work was approximately the same between the two co-authors, hence there is no seniority of authorship.

An acknowledgment of appreciation is due Dr. J. T. Patterson, of The University of Texas, for his helpful suggestions throughout the course of the experiments.

LITERATURE

As has previously been stated, the work on reverse mutations has not been great. In plants, Emerson (1917), Baur (1930) and Demerec (1928) report reverse mutations in Maize, Antirrhinum and Delphinium, respectively. Demerec (1928) reports frequent reversion of unstable genes of *Drosophila virilis*. Stern (1930) reports the spontaneous simultaneous reversion of yellow and "kurtz" (short bristles) in *Drosophila melanogas-*

ter. By far the greater number of reverse mutations, however, have resulted from irradiation. Timofeeff-Ressovsky (1928, 1929a, 1929b, 1930a, 1930b, 1933) has succeeded in securing somatic mutations in different directions in studies of w, w^e and W, and has secured genic reversions of about seven different loci in *Drosophila melanogaster* through irradiation. Patterson and Muller (1930) report reversions of sc and f in *Drosophila melanogaster* under the influence of irradiation.

TECHNIQUE

Flies from the regular stocks of *Drosophila melanogaster* at the University of Texas were used in this study. Ten recessive mutant genes, all lying within the X-chromosome, were selected for a thorough investigation of each. These genes were yellow body color (y), scute bristles (sc), apricot eye color (w^a), echinus eye (ec), cut wings (ct), vermilion eye color (v), miniature wings (m), garnet eye color (g), forked bristles (f) and carnation eye color (car). At the beginning of the experiment flies containing six of the above characters were used, but these proved so infertile, especially after irradiation, that it was thought advisable to use fewer characters at a time, so the number was reduced to three characters in a fly. In the experimental series males possessing the genes to be studied were x-rayed with a dose of approximately 3975 *r* units and mated to virgin females containing attached X-chromosomes or homozygous for the characters in question. In the first case the F_1 males would receive the treated X-chromosome of their father and would reveal any reverse mutations that had occurred. In the case of the homozygous females the treated X-chromosome would go to the F_1 females, but, since all the characters are recessive, any reverses could be detected as they would act as a dominant to their mutant allelomorphs. Control experiments were also carried on under the same conditions except that no irradiation was given.

In order to be sure that all suspected reverse mutations were not due to another gene acting as a suppressor or to some chromosome abnormality they were tested in the following manner. Whenever a fly was found that was phenotypically normal in respect of any of the characters it was supposed to have inherited, it was bred for several generations to be sure the change was in the germ plasm. Then males showing the supposed reverse mutation were mated to females of the wild type or bearing convenient markers. The amount of crossing-over was determined in the F_2 and compared to the standard cross-over values. If crossing-over was normal without the reappearance of the mutant character in question, it was evident that a reverse mutation had occurred. Had the effect been due to a suppressor it would have been crossed out, allowing the mutant gene to be expressed, while a suppressor accompanied by an inversion would have been detected in the cross-over counts.

Experimental Results and Discussion

As previously stated the distribution of work was approximately the same between the two co-authors. The genes studied and reverse mutations found by each author are given below.

One of us (Johnston) worked with the genes sc, ec, ct, v, g, f. Males bearing several of these genes were crossed to yellow females with attached X-chromosomes and the male offspring were examined in the first generation. From an examination of 355,326 irradiated genes, she secured reverses of the following genes: two untested scute, no echinus, one cut, one vermilion, four untested garnet, and five forked, two of which were untested. In addition she found an apparent reverse of vermilion which bred true for several generations, but when subjected to the cross-over test vermilion again appeared. It was evident that a sex-linked suppressor was present and it was later located at the locus of white.

The other of us (Winchester) worked with the genes y, sc, w^a, m, f, car. Males carrying some of these genes were mated to females homozygous for the same characters. The F_1 females were examined and the following reverses were found in a total of 358,675 irradiated genes: one yellow, one scute, no apricot, two miniature, six forked with two of them untested, and one untested carnation. Homozygous females were used in this work in order to be able to detect any reverses which might occur accompanied by a sex-linked recessive lethal, which could be detected only in females as males of this type would never mature into adult flies. This condition is often found in the case of direct mutations, but no cases of this kind was found among the reverses. An autosomal partial suppressor of scute was also found.

Considering the results as a whole we find from a total of 713,000 genes examined in the x-rayed series, twenty-four reverse mutations were found at eight of the ten loci studied. In approximately the same number of genes in the controls, no reverse mutations were found. However, of the twenty-four which were found, twelve proved to be sterile or so inviable that they could not be bred further, a condition which frequently follows heavy irradiation. Thirteen phenotypic reverses proved to be genic, since they bred true for several generations. In order to be sure that the effect was not due to a suppressor they were subjected to the cross-over test. Twelve proved to be true reverses, while one (a supposed reverse of vermilion) was due to a suppressor. It is apparent from this result that the great majority of phenotypic reverses are true genic mutations, so the twelve apparent reverses which failed to breed will be included in the discussion on the basis of the probability that about eleven of them are genic mutations. Table I gives a complete record of all reverse mutations found. This table also includes the results of Timofeeff-Ressovsky (1930) on the same loci, but with a heavier treatment with x-rays. Since Hanson (1930), Oliver (1930) and

TABLE I

REVERSE MUTATIONS INDUCED THROUGH X-IRRADIATION OF RECESSIVE GENES OF THE X-CHROMOSOME

Gene	Johnston and Winchester (3975 *r* units)		Timofeeff-Ressovsky (4800 *r* units)		Per cent. mutations on the basis of 3975 *r* units	
	No. flies examined	Reverse mutations	No. flies examined	Reverse mutations	Johnston-Winchester	Timofeeff-Ressovsky
y	69,923	1	6,354	0	.0014	.0000
sc	101,042	3(2?)	14,550	3(1?)	.0030	.0171
w^a	69,302	0	.....	.....	.0000	.....
ec	57,323	0	14,550	0	.0000	.0000
ct	57,323	1	9,788	0	.0017	.0000
v	61,119	1(?)	16,142	1(?)	.0016	.0051
m	39,923	2	.....	.....	.0050	.....
g	57,323	4(?)	9,788	0	.0070	.0000
f	130,421	11(4?)	16,142	2	.0084	.0102
car	69,302	1(?)	.....	.....	.0014	.....
Total	713,001	24(12?)	87,314	6(2?)	.0034	.0057

others have shown that there is a direct proportionality between the intensity of the dose and the mutation rate, the last two columns compare the results as calculated on the basis of 3975 *r* units. It can be seen that the results compare favorably, the greatest difference being at the locus of scute, which variation, however, is still within the limits of experimental error.

Of the genes studied, forked seems to revert most frequently. Eleven reverses were found of this gene (nine complete, one bilateral fractional, and one partial reverse which produces bristles more nearly normal than forked). Patterson and Muller (1930) find a higher rate of reversion of this gene when larvae are treated rather than adults. According to the calculations presented in their paper, six reverses were found in approximately 30,000 flies descending from larvae treated with 1325 *r* units. They also found two reverses among 14,496 flies descending from adult males treated with the same dose, but one of these was a fractional which failed to breed true and

the other was a partial reverse. More recently Timofeef-Ressovsky (1933) has reported seven reverses of forked among 29,000 flies resulting from adult males treated with 4800 *r* units. Calculated on the basis of 3975 *r* units this is .0199 per cent. as compared to .0102 per cent. in his previous paper (1930) and .0084 per cent. found in the experiments described in this paper. However, he fails to indicate whether the mutations were complete, partial, or fractional, or what breeding tests were used, so we have no accurate basis for comparison with the other results.

Another interesting comparison might be made between the direct and reverse mutation rate under the influence of irradiation. W. G. Moore (unpublished data) has been working in this laboratory on a thorough analysis of the direct mutation rate. Table II shows his

TABLE II

DIRECT AND REVERSE MUTATIONS OBTAINED BY IRRADIATION OF ADULT MALES
(Dosage—3975 *r* units)

Gene	Direct Mutations (W. G. Moore)		Reverse Mutations (Johnston-Winchester)		Per cent. Mutations	
	No. flies examined	Mutations	No. flies examined	Mutations	Direct	Reverse
y	11,620	3	69,923	1	.0258	.0014
sc	11,620	6	101,042	3	.0516	.0030
w^a	11,620	0	69,302	0	.0000	.0000
ec	11,620	18	57,323	0	.1548	.0000
ct	11,620	0	57,323	1	.0000	.0017
v	11,620	6	61,119	1	.0516	.0016
m	11,620	3	39,923	2	.0258	.0050
g	11,620	6	57,323	4	.0516	.0070
f	11,620	6	130,421	11	.0516	.0084
car	11,620	0	69,302	1	.0000	.0014
Total	116,200	48	713,001	24	.0413	.0034

results from irradiation of adult males as compared to the reverse mutation rate as calculated on the basis of 3975 *r* units. As a whole it can be seen that direct mutations are about twelve times as frequent as reverse for

the genes in question. Also, while there is a variation in both the direct and reverse mutation rate, there seems to be no relation between the two. For instance, echinus was found most frequently as a direct mutation, but was never found as a reverse; and forked, which leads the reverse mutations, fails to stand out above the group in direct mutations.

Summary and Conclusions

(1) Reverse mutations were found of the genes y, sc, ct, v, m, f, and probable reverses of g and car which could not be tested. No reverses were found of w^a and ec.

(2) Of the genes studied, forked reverts most frequently, about once in 12,000 flies, which is about one sixth the frequentness of direct mutations of this gene.

(3) It is evident that, in the case of the genes studied, reverse mutations as a whole occur much less frequently than direct mutations of the same loci; the ratio being about 1:12.

(4) There is a great variation in the frequentness of reversion of the different genes, which, however, bears no apparent relation to the frequentness of direct mutations at the same loci.

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THE PRODUCTION OF TRANSLOCATIONS IN DROSOPHILA

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INTRODUCTION

DURING the course of our study on the genetic effects of the duplication of pieces of the X-chromosome in *Drosophila melanogaster,* we have found it necessary to have available different types of translocations. After considering the various ways that have been employed to obtain translocations in this fly, we decided that the following method was the most advantageous. This method was developed by one of us (Stone) in connection with his previous work with Dr. H. J. Muller, who suggested that the use of recessive gene markers for each of the autosomes would be better than the usual procedure of employing dominant markers for these chromosomes.

The type of female to which the x-rayed wild-type male is mated has attached X-chromosomes that are homozygous for the mutant gene yellow, and the three pairs of autosomes are homozygous for brown, ebony and eyeless, respectively. The F_1 heterozygous wild-type males are backcrossed individually to this same type of female. Examination of the F_2 cultures will reveal whether or not translocations are present. If no translocation has occurred, there will be random assortment; but if one is present, the chromosomes involved will segregate together, except in cases where hyperploids or hypoploids live. It is clear that eleven different types of translocations can be detected by this method, and these are as follows:

T_A 1–2 (X–II) males non-brown; females brown.[1]
T_A 1–3 (X–III) males non-ebony; females ebony.

[1] This nomenclature is in accord with that devised by Demerec and Bridges, using sub-A to indicate those translocations found at the Austin laboratory. See "Drosophila Information Service, No. 1."

T_A 1–4 (X–IV) males non-eyeless; females eyeless.
T_A 2–3 (II–III) flies either non-brown, non-ebony or else brown, ebony.
T_A 2–4 (II–IV) flies either non-brown, non-eyeless or else brown, eyeless.
T_A 3–4 (III–IV) flies either non-ebony, none-eyeless or else ebony, eyeless.
T_A 1–2–3 (X–II–III) males non-brown, non-ebony; females brown, ebony.
T_A 1–2–4 (X–II–IV) males non-brown, non-eyeless; females brown, eyeless.
T_A 1–3–4 (X–III–IV) males non-ebony, non-eyeless; females ebony, eyeless.
T_A 2–3–4 (II–III–IV) flies either normal or else brown, ebony, eyeless.
T_A 1–2–3–4 (X–II–III–IV) males normal; females brown, ebony, eyeless.

The classes of flies for each of the eleven types of translocations appear as indicated above, except in those cases in which abnormal chromosome complexes survive as hypo- or hyperploidy. Usually both do not survive, so that the translocations are detected anyway. There are two disadvantages to this method: (1) in case the translocation involves the Y-chromosome it will not be detected, because the treated Y-bearing sperms fertilize those eggs that develop into females, and the F_1 females are not tested; (2) translocations involving the X-chromosome and accompanied by a sex-linked lethal will not produce a viable male zygote and hence can not be tested. This, however, is not a serious disadvantage for our work.

From January to June, 1933, the senior author and the first two junior authors carried on an extensive experiment, designed to obtain as many translocations as possible. We x-rayed the wild-type males with a dosage of 4,452 *r* units and continued the experiment until ten thousand fertile F_2 cultures had been obtained. A total of 13,475 individual F_1 males were mated before this goal was reached. The experiment yielded 1,992 apparent

TABLE 1

Fertile F_2 Cultures	T_A 1–2	T_A 1–3	T_A 1–4	T_A 2–3	T_A 2–4	T_A 3–4	T_A 1–2–3	T_A 1–2–4	T_A 1–3–4	T_A 2–3–4	T_A 1–2–3–4
10,000	146	187	14	1,236	50	55	71	3	6	22	2
Per cent.	1.46	1.87	.14	12.36	.5	.55	.71	.03	.06	.22	.02

translocations, which were distributed among the eleven expected types as given in Table 1.

The first six types of translocations have been used in our studies, while the remaining five have been discarded. Any one of the latter group can be produced by crossing over between known combinations of the first group, thus avoiding the necessity of analyzing such complex translocations.

Results of Genetic Tests on Translocation Stocks

The stocks developed from the first six types of translocations, listed in Table 1, are being investigated with reference to the following points: (1) homozygosity, (2) fertility, (3) points of breakage and (4) hyperploidy. The results obtained in these studies up to the present time are summarized in Tables 2 to 7.

TABLE 2

Homozygosity

Types	Number tested for homozygosity	Number live homozygous	Per cent. live homozygous	Number fertile	Per cent. fertile homozygous	Number sterile	Undetermined fertility
T_A 1–2	57	30	52.6	21	91.3	2	7
T_A 1–3	71	30	42.2	27	90.0	3	0
T_A 1–4	14	14	100.0	13	100.0	0	1
T_A 2–3	120	19	15.8	19	100.0	–	–
T_A 2–4	33	23	69.6	15	88.2	2	6
T_A 3–4	37	18	48.6	16	88.8	2	0

In Table 2 are shown the results obtained on the number of cases that have been tested for viability and fertility in the homozygous condition for each of the six types of translocations. There is one point, not revealed in the

tabulated data, that should be mentioned. This is that one of the two stocks listed as sterile in homozygous in the sixth type (T_A 3–4) lives homozygous in females only.

TABLE 3

TRANSLOCATIONS INVOLVING CHROMOSOMES I AND II (T_A 1–2)

Stock number	Viable homozygous	Fertile homozygous	Break in I	Break in II	Hyperploid viable
105	not tested		*sd–f*	?	yes
124	" "		*ct–v; g–pl*	no *apl* genes involved	"
12,59	" "		*sd–f*	no *apl* genes involved	"
96,150	" "		right of *car*	no *apl* genes involved	"
7,163	no	—	" " "	left arm	no
162	yes	yes	" " "	" "	"
17	not tested		" " "	*pr–c*	"
50	no	—	" " "	" "	"
69	yes	yes	" " "	" "?	"
20,99	no	—	" " "	?	"
146	yes	yes	" " "	"	"
65	"	"	" " "	beyond *al* or *sp*	"
68,153,166	no	—	" " "	" " " "	"
81	yes	no	" " "	" " " "	"
94,104	no	—	" " "	left of *al*	"
118	yes	yes	" " "	right of *sp*	"
135	"	not tested	" " "	" " "	"
148	no	—	" " "	" " "	"
113	yes	yes	" " "	*dp–b?*	"
164	no	—	" " "	" "	"
159	yes	yes	" " "	*c–px*	"
160	not tested		" " "	*b–pr*	"
76	yes	yes	" " *f*	*pr–c*	"
92	"	no	" " "	" "	"
79,107	"	not tested	" " "	right of *sp*	"
1	"	yes	*sc–oc*	*al-dp* or left of *al*	"
14	"	"	" "	right of *sp*	"
111,141	no	—	" "	" " "	"
19	yes	yes	" "	*c–px*	"
155	no	—	" "	" "	"
21	"	—	" "	left arm	"
55	yes	not tested	" "	" "	"
147	"	yes	" "	" "	"
57	"	"	" "	left of *al*	"
157	yes	not tested	" "	*pr–c*	"

Table 3 gives the results of investigating translocations between the X and the II chromosomes for homozygosity and fertility *c* point of breakage and hyperploidy.

For the sake of convenience, cases showing breaks in the same region and with the same homozygosity are listed together. In addition to the homozygosity tests listed in Table 3, there are twenty-one translocations not analyzed for location of the breaks, of which eleven did not live homozygous, eight were both viable and fertile homozygous, and two were viable homozygous but of undetermined fertility. Forty-four translocations were studied for location of the point of breakage. The data show that only five breaks took place between the loci of ocelliless at 20.1 and forked at 56.7. Eleven of the remaining breaks were between scute and ocelliless, and twenty-nine were to the right of forked or carnation. In the X-chromosome, therefore, the majority of breaks occurred in the end regions. In the II chromosome, sixteen breaks were either to the left of aristaeless or to the right of speck, and six were between purple and curved. Thus we see that the free and spindle fiber end regions in the II are also heavily represented. Six of the T_A 1–2 translocations produced viable hyperdiploid (for the X) females which were presumably hypoploid for the part of the II.

TABLE 4

TRANSLOCATIONS INVOLVING CHROMOSOMES I AND III (T_A 1–3)

Stock number	Viable homozygous	Fertile homozygous	Break in I	Break in III	Viable hyperploids
60	yes	yes	*sc–ec*	left of *h*	no
169	no	—	*ec–ct*	e^s–*ca*	"
8, 96, 191	yes	yes	right of *f*	*st–p*	"
5	"	no	" " "	"	"
140, 170, 175	no	—	" " "	"	"
143	not tested	—	*y–sc*	—	yes
144, 188	" "	—	*sc–ec*	—	"
18, 56	yes	yes	"	—	no
19	no	—	"	—	"
52	"	—	*g–f*	—	"
6, 32	yes	yes	right of *f*	—	"
194	"	"	" " "	left arm	"
9, 20, 34, 35, 51	no	—	" " "	—	"
189	not tested	—	right of *car*	—	yes
66	yes	yes	—	right of e^s	no
176	no	—	—	*p–cu*	"

In these cases the II chromosome was tested with the *apl* (*al dp b pr c px sp*) genes for hyper- or hypoploidy, but no *apl* genes were found to be involved in any of them. In one translocation, number 59, a mutation to *dp* was discovered.

In Table 4 are listed twenty-seven cases which represent samples of the X–III chromosome type of translocation. Twenty-three cases were tested for homozygosity, and eleven were found to live in the homozygous condition. Ten of these are fertile. In addition to those

TABLE 5

TRANSLOCATIONS INVOLVING CHROMOSOMES I AND IV (T_A 1–4)

Stock number	Break in X	Break in IV	Viable and fertile homozygous females	Viable hypoploid females	Hyperploids							
					Females				Males			
					viable		fertile		viable		fertile	
					L	R	L	R	L	R	L	R
4	*sd–f*	—	yes	?	yes	yes	no	yes	no	yes	—	no
8	*m–g*	*ey bt*–sp. f.	"	no	"	"	yes	"	"	no	—	—
9	*rb–cv*	"	"	"	"	"	"	no	yes	"	no	—
10	left of *y*	"	"	"	—	—	—	—	—	—	—	—
12	Complicated (see text)		"	—	—	—	—	—	—	—	—	—
13	*fu–car*	—	"	yes	yes	yes	no	yes	no	yes	—	no

listed in the table, forty-eight other stocks were also tested for homozygosity, but the points of breakage have not as yet been determined. Nineteen of the forty-eight cases are viable in homozygous, and seventeen of these are fertile.

The most striking feature, of the breaks in the twenty-seven tested cases, is the fact that the X-chromosome is broken beyond the locus of forked in seventeen of these cases. The point of breakage in the III-chromosome has been definitely determined in eleven cases, and in seven of these it occurred between the loci of scarlet and pink.

The hyperploids live in only four of the twenty-seven stocks.

In Table 5 are listed six cases of translocations involv-

TABLE 6

TRANSLOCATIONS INVOLVING CHROMOSOMES II AND IV (T_A 2–4)

Stock number	Viable homozygous	Fertile homozygous	Break in II
47	no	—	left of *al* or right of *sp*
9	undetermined	—	left of *al*
2	"	—	*al–dp*
8	yes	yes	*dp–b*
5, 52	"	"	*b–pr*
41	"	"	" ?
28, 35	"	undetermined	"
54	"	"	" ?
37	undetermined	—	"
12, 27, 45, 57	no	—	"
44	undetermined	—	left arm
33	no	—	" "
4, 13, 21, 26, 40, 50	yes	yes	*pr–c*
11, 53	"	undetermined	"
51	"	yes	" ?
1, 7, 29, 56	no	—	"
30	yes	yes	*c–px*
34	"	undetermined	*px–sp* ?
6, 23	"	no	right of *sp*

ing the I and IV chromosomes. They represent breaks in various regions of the X-chromosome. Five are simple breaks, and one, No. 12, is a complex case. In regard to the simple breaks, it can be stated that the following hyperploids, 4–L, 9–R, 13–L, greatly resemble, and occur

in the cultures at about the same frequency as triple-X females.

No. 12 is a double deletion, accompanied by translocations. The main deleted section, with breaks between the loci of scute and echinus on the left and between those of

TABLE 7

TRANSLOCATIONS INVOLVING CHROMOSOMES III AND IV (T_A 3–4)

Stock number	Viable homozygous	Fertile homozygous	Breaks in III
52	yes	yes	left of *h*
22, 34, 44	no	—	"
6	yes	yes	At *h*
23	female only	no	"
13	no	—	*h–th*
8, 12	yes	yes	*th–st*
7, 14, 31, 36, 58	"	"	*st–p*
45	"	no	"
4, 35, 40, 46, 54, 56	no	—	"
37	"	—	*p* ?
27	yes	yes	*p–cu*
9	"	"	*cu–sr*
20	no	—	"
43	"	—	*cu–sr–e*^{s}
2, 28	yes	yes	*e*^{s}*–ca*
5, 39, 51, 60, 30	no	—	"
1, 49, 59	yes	yes	right arm
24	"	"	undetermined

garnet and scalloped on the right, is translocated to the IV, with the further complication that the region including the locus of cut is deleted and attached to the II. The remainder of the X-chromosome has its own spindle fiber.

Both males and females hyperploid for the cut locus are viable and fertile. Females hypoploid for this locus are viable and fertile, as are also females hyperploid for the independent fragment of the X-chromosome. Finally, females hyperploid for the piece attached to the IV are viable, but resemble the triple-X and are sterile.

In addition to these six cases, eight other apparent translocations of the X to the IV were found, but genetic and cytological analyses show that these represent fusions in the spindle fiber region.

Thirty-seven cases of translocations involving the II and IV chromosomes have been studied (Table 6). Twenty-three out of the thirty-three tested were found to be viable in homozygous. Fifteen of these are fertile, two are sterile, and six are still undetermined. A large majority of the breaks in the II chromosome occurred at two regions; eleven between the loci of black and purple in the left arm, and thirteen between the loci of purple and curved in the spindle fiber area.

There were thirty-seven cases of translocation involving the III and IV chromosomes that have been studied (Table 7). Seventeen of these are viable in homozygous, but one in females only (No. 23). All except two are fertile. As in the case of the II-chromosome, a majority of the breaks in the III-chromosome also occurred at two regions; twelve between the loci of scarlet and pink, near the spindle-fiber area, and seven between the loci of sooty and claret in the right arm. No. 30 is an interesting case, in that it proved to be a mutual translocation, in which the break in the IV-chromosome occurred between the locus of eyeless and the spindle-fiber end, and the break in the III occurred between the loci of white-ocelli and rough. It also represents the only proved case in which hyperploids are viable.

Discussion

From *a priori* reasoning, several factors should determine the relative rates of the various types of transloca-

tions: (1) Length of the chromosomes involved, (2) position of the chromosomes within the cell, (3) regional affinity either for breakage or for a non-homologous chromosome, (4) size of the cell. If there were a random distribution of breaks along the chromosomes, then we could accept length as the main factor in controlling the type rate of translocations, as the data in Table 1 suggest. Tables 3 to 7 show, to the contrary, that the majority of breaks occur either at the free or spindle fiber ends of the chromosomes. We consider II and III as each having four "ends," two free and two spindle fiber.

If the chromosomes in the mature sperm at the time of x-raying lie with their ends, spindle fiber and free, associated in a definite region of the cell, then most of the breaks would of necessity take place at the ends of these chromosomes. It is no radical departure from cytological observation to assume polarization of the chromosomes, so that the ends lie together. Similar phenomena occur in the bouquet stage of meiosis and in the salivary glands and other somatic cells. In the former, the free ends of the chromosomes are associated; in the latter, the spindle fiber ends. An association of both free and spindle fiber ends, therefore, would not be a too radical assumption. Since the breaks are so markedly grouped in definite regions, we believe that most translocations, though not necessarily all, occur by an attachment followed by breakage. By this method either a non-mutual translocation, mutual translocation or fusion may result, depending on whether one, both or neither of the chromosomes break. If the chromosomes break first, then reattach, we should have to assume a regional affinity for breakage in order to explain our experimental distribution of translocations. In this case, the position of the chromosomes within the cell would be of little significance.

Since types T_A 1–2 and T_A 1–3 are already selected against lethals in the X-chromosome, most of the data in the table represent the effect of lethals in the autosomes,

except in cases where the homozygous female is inviable although the male is viable (*e.g.*, bb-deficiency). The IV-chromosome seems to have no lethal effect. In Table 2, the viability of a translocation involving one of the large autosomes varies from 42.2 per cent. to 48.6 per cent. to 52.6 per cent. to 69.6 per cent. In combining the effects of the II and III in type T_A 2–3, we should expect approximately 27.7 per cent. to be viable, but only 17.6 per cent. to be both viable and fertile, calculated on the basis of fertility of T_A 2–4 and T_A 3–4. Compare this with the actual 15.8 per cent. We can infer from this and from an examination of Tables 3 to 7 that there is no positive correlation between the region of breakage and lethals induced at the time of breakage.

All hyperploid females are viable in type T_A 1–4 (Table 5), but any form of hyper- or hypoploidy is rare in all other types of translocation. Therefore, the large autosomes, not the X, are responsible for the comparative absence of hyper- or hypoploidy in all these translocations.

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SHORTER ARTICLES AND DISCUSSION

PROFESSOR WRIGHT ON THE THEORY OF DOMINANCE

In 1928, as the result of some calculations of the selective intensity, acting on modifying factors, capable of modifying the degree of dominance exhibited by deleterious mutations, I put forward the supposition that the great excess of recessives among observed mutants was the result of many of them having been progressively modified to the recessive condition during a very long period of previous occurrence of the same mutations.

At that date I was unaware of the very large amount of evidence now available to geneticists, as to the modifiability of the degree of dominance, and of the very beautiful examples afforded by polymorphic species, where the variant forms have become dominant to the type, under selection in the opposite direction. The existence of this evidence much diminishes the interest of such rough attempts to estimate the relative intensity as are possible by general reasoning. My only strong reason, however, at that time for proposing that dominance phenomena were subject to evolutionary modification was that a selective intensity could be demonstrated, of a magnitude, which, in the periods available, was sufficiently powerful, unless some unknown cause opposed it, to bring about appreciable modification in the reaction of species to the deleterious mutations which have for long been occurring in them. For an account of the more general evidence on the subject, which was rapidly brought to my notice through the kindness of a number of geneticists, I may refer the reader to a more recent paper, "The Evolution of Dominance."[1]

Following the original paper, however, in May, 1929, Professor Sewall Wright, who had perhaps overlooked or misunderstood the calculations in my paper, put forward some calculations of his own, expressed in a different notation, which, for the general case, gave a result identical with mine. For the special case of a single and completely dominant modifier, which he chose for more detailed consideration, he obtained results apparently unfavorable to my theory, in that the selective intensity calculated was not only small, of the order of the mutation rate of the mutating gene, but decreased progressively to zero with the ad-

[1] *Biol. Reviews*, vi: 345–368.

vance of the process. This result, however, as I pointed out in a short note published the following November, was due to an error in the algebra, the real selective intensity in the case chosen by Wright increasing without limit as the dominant modifier becomes more and more numerous.

In a paper published in January, 1934, Wright accepts my correction to his calculation. He does not refer to its history, or to the fact that, in 1928, I had already shown two facts respecting the selective intensities arrived at. (i) That these depended greatly on the viability of the heterozygote to be modified, and (ii) in cases where this viability is near to the normal, that modification would take place at about one five-thousandth of the rate that at which a population composed wholly of heterozygotes could be modified. For periods of the order of 500,000 generations, therefore, substantial selective modifications of the heterozygote is a necessary consequence of the calculations, upon the accuracy of which we now seem to be agreed.

The importance of the viability of the heterozygotes arises from its influence on their frequency. In putting forward the theory, I postulated only such frequency as could certainly be maintained by mutation against counter-selection. More recent researches into the frequency with which mutant heterozygotes can be found in collections from wild populations suggest that they are in fact much more abundant than the theory suggests. If this is so, the selective process will be proportionately more rapid. The point is to be noted as Wright has asserted that he is discussing a case especially favorable to my views, while in fact restricting himself to the minimal postulates in its favor.

In his recent restatement of his opinion Wright shows that the modifier will not increase in frequency if its increase is opposed by a mutation rate just double that of the primary mutation. This is obvious from the corrected formulae given in my note of 1929, and establishes the unimportant fact that dominance modification will not be affected by modifiers, the increase of which is opposed by a mutation-rate of this magnitude. This does not prevent its being effected by modifiers whose mutations are either favorable, or, if unfavorable, of a lower frequency. It has long been recognized that the mutation-rates of those mutations which make themselves available for study, by occurring in culture, must be among the largest which occur in the species. It is among mutations of this kind that nearly complete

recessiveness is known to be the rule. How far up the scale of rarity this rule holds we do not know, but it is clear that the supposition of adverse mutations only serves to exclude a group of modifiers the mutations of which are not only adverse, but exceptionally frequent. The effect, such as it is, is, of course, counterbalanced if modifiers with equally high mutation rates, but in a favorable direction, are assumed to be equally numerous.

Professor Wright, however, draws a wider but less legitimate inference. He quotes me as saying elsewhere that, "For mutations to dominate the trend of evolution it is thus necessary to postulate mutation-rates immensely greater than those which are known to occur," and seems to infer that by this I imply that magnitudes of the order of mutation rates, say 1 in a million per generation, are to be ignored in every context. Nothing could be further from the truth. In the quotation, I was discussing theories of evolution, such as Lamarckism and Orthogenesis, which purport to give an explanation of evolutionary change, by means of hypothetical causes supposed to produce germinal modifications. These theories are open to the objection that mutation rates of the order of 1 in a million can bring about nothing *if opposed even by very minute counter-selection.* If evolution is to proceed in any direction, to which the selective action of differential death and birth rates is in the slightest degree antagonistic, the supporters of these theories must postulate, I was asserting, much higher mutation rates than those with which geneticists are familiar. In the case of modifiers which improve the viability of a rare heterozygote, it is my theory that these will increase in frequency through the greater viability that they induce, not that they will increase in frequency by mutation in opposition to the selective tendency. In fact, apart from the exceptional case stressed by Wright, it is clear that here also mutation rates have little direct influence on the process.

Professor Wright mentions another argument which should be answered, as it evidently weighs with him, though the fallacy is a simple one. He says, "There should always be other evolutionary pressures of greater magnitude acting in one direction or the other," and appears to think that this implies that a selective intensity of lesser magnitude has therefore no effect.

Let us suppose that all modifiers of dominance are influenced one way or the other by selections other than that caused by their effect as modifiers. Professor Wright does not propose that

the unfavorable selections are more numerous or more intense than those which are favorable. If the selective intensities due to the other causes which Wright postulates are represented in a frequency diagram, the mean will therefore be at zero. Let us take x as a typical value of the variate in this distribution, measuring x as positive when the selective tendency is favorable to dominance modification, and negative when it is unfavorable. The average value of x is then zero. Suppose that the small selective effect produced by the modification of the heterozygote is represented by a small, but positive, quantity, *a*, then in each case the net selective intensity in favor of dominance modification, whether positive or negative, will be $a + x$; and the aggregate effect of all the modifiers will be found by adding together this quantity for each of them. To this sum it is clear that the component x contributes nothing, since the positive and negative values of x balance each other. We are left, therefore, with the sum of the positive values *a*, each of which is favorable to dominance modification; exactly the same result as if we had ignored the "other evolutionary pressures of greater magnitude" from the start. The fallacy of Professor Wright's reasoning seems to be simply that by concentrating his attention only on the question of whether a gene is finally exterminated or not, he ignores the much more important question of the rate at which it approaches extermination. This rate is affected for all genes capable of modifying the heterozygote, while the balance in favor of fixation or extermination is only turned in the case of that minority for which the value of x lies between o and $-a$.

The fallacy may be stated in another form, by stressing the improbability, when *a* is small, of a number chosen at random from the population of selective intensities falling between the limits o and $-a$. But this improbability does not adhere to the conclusion that a selective intensity, however minute, affecting all modifiers consistently in the same direction, will exert an effect proportionate to its magnitude, whether these modifiers are affected by other selective agencies or not, provided that these agencies are not in a conspiracy to oppose dominance modification.

In fact, it would do so even if it happened that there were a gap in the frequency distribution, so that none occurred in the region between o and $-a$.

Professor Wright's recent allusion to the subject was but a preface to his own interesting speculations on the physiological causation of dominance. It had, perhaps, achieved its purpose when he could write, "If this hypothesis is untenable what alternative is there?" If, however, Professor Wright's views can only be made plausible, by the exclusion of all alternatives, he must find other objections to the selection theory more weighty than those he has revived.

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CROSSING-OVER OF SEX CHROMOSOMES IN DROSOPHILA

Two types of structural change take place occasionally between the X and Y chromosomes of *Drosophila melanogaster* under normal conditions, the attachment of X with the long arm of the Y in males (XY′ of Stern, 1929) and the detachment of the attached X's (XX) in females. I have pointed out (1931) that the first type of change, like that giving rise to half-mutants in *Oenothera,* resembles crossing-over in its consequence, exchange of segments and in one of its antecedent conditions, homology at the point of exchange, while it differs from normal crossing-over in the rarity of the event and the non-homology of adjoining segments.

I had suggested that X and Y normally paired in the male by two chiasmata which, occurring in a segment with no genes (now described as the inert region) and by reciprocal crossing-over, would give no genetical results. I have since advanced cytological evidence in favor of this view (1934).[1] I supposed then that XY arose by single crossing over the wrong way round between X and Y, since an "inverted chiasma" could not be reciprocal and would therefore give an effective change of structure.

The clear cytological demonstration by Kaufmann (1933) that the second type of change agrees in its observable consequences with the expectation on the assumption of crossing-over makes it worth while to consider the whole question in

[1] Philip (1934) has now found genetical evidence to the same effect.

greater detail. Kaufmann finds that when the XX chromosome becomes detached it yields two new types of chromosome, consisting the one of an X fused with the short arm of Y (XY^s), the other of an X fused with the long arm of Y (XY^L, which is presumably the same as XY′ of Stern). He therefore infers an exchange or crossing-over between XX and Y. On the basis of the observations concerned, this might have occurred between either the short arm or the long arm of Y and a corresponding segment in one of the X's. It had seemed to me that the homologous region of Y must be in its long arm both from general comparison of chromosome complements in *Drosophila* and from the position of the "bobbed" inhibitor in the long arm of Y.

Kaufmann, on the other hand, prefers to suppose that the short arm is concerned and on two grounds. First, no crossing-over with Y occurs between the spindle attachment and "bobbed" in the X of XXY females. This objection does not seem to be insuperable. Any cross-over between X and Y might occur reciprocally as in the males, and moreover might occur equally well if the short arm were the homologous segment.

The second objection is more serious: 'Homologous pairing and simple crossing-over would give XY′ if the pairing segment were in the short arm of the Y, but exchange between the long arm of the Y and the proximal region of the X could not be expected to furnish the XY′ chromosome, either on a basis of "homologous" pairing or on the basis of inverted pairing with an inverted chiasma suggested by Darlington to explain this chromosomal aberration.' This depends on the pairing and crossing-over properties we assume at the attachment chromomere itself. I had assumed that the attachment chromomeres ("polar granules") paired in an inverted way and that crossing-over occurred between them and the adjoining non-homologous chromomeres, and this hypothesis is perhaps sufficient.

But there is some evidence to suggest a slightly different view, namely, that the crossing-over might occur *within* the attachment chromomere. We now know that this body has special mechanical functions in relation to crossing-over, terminalization and anaphase separation, and that these functions are uniform in all the chromosomes of a complement. The staining properties of the attachment chromomere are also special and uniform. It seems therefore that the characteristic pairing properties of

the genes, depending upon specificity and polarity, are not necessarily properties of the attachment chromomere. Further, one of the two ways of defining a gene is by its indivisibility in respect of crossing-over. An attachment chromomere may, if non-specific, be compound.

These views are suggested by the behavior I found in *Agapanthus* (1932) and also by various observations on *Drosophila*. First, Stern and Ogura (1931) found the results of crossing-over between the pairing segments of two Y's in XY′ + Y males. Here the whole of the pairing segment of Y's must be represented in triplicate *except the attachment chromomere*. In such an individual Y would pair without competition at this point alone and might therefore pair only there in some nuclei, so that any crossing-over that occurred would be non-reciprocal and genetically effective. The pairing situation is precisely the same as in the XX + Y female in which Kaufmann has studied detachment.

Secondly, Friesen (1933) has induced crossing-over by irradiation in the autosomes of male *Drosophila*. (Whether the sex chromosomes can be reconstituted in the same way he does not state.) Analysis of his data shows that crossing-over occurs in segments containing the spindle attachment chromomere and not in other segments, with only two exceptions. This agrees with the third body of evidence, my cytological inference (1934) that intimate association of the autosomes occurs only at the spindle attachment in male *Drosophila*. It also supports the assumption that crossing-over may normally occur between chromosomes that are only associated at this point.

I conclude therefore that there is no difficulty in supposing that the pairing segment lies in the long arm of the Y in *Drosophila melanogaster* (although it extends to both arms in *D. pseudo-obscura*), but that exceptional crossing-over occurs at or adjoining the spindle attachment in both male and female *Drosophila*, owing to the anomalous properties of the attachment chromomere, which promise interesting possibilities for further investigation.

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RELATION BETWEEN THE EFFECT OF A GENE AND ITS POSITION IN THE SYSTEM

STURTEVANT (1925) discovered that two bar genes lying in the same chromosome are more effective than the same two genes lying in different chromosomes. This discovery established the phenomenon of the effect of position on the properties of the gene bar. Muller and Altenburg (1930), Dobzhansky (1932, 1933) and Dobzhansky and Sturtevant (1932) used the position effect hypothesis as one of several possible explanations for the gene changes observed near the breakage points in translocations and duplications. The existence of position effect is not established in any of these cases, except in that of bar.

We have studied nineteen translocations in *Drosophila melanogaster* involving the fourth chromosome, on one hand, and the second, third, X or Y chromosomes, on the other. An unexpected phenomenon is observed if these translocations are made heterozygous for the fourth chromosome recessive gene *cubitus interruptus* (*ci*). Ten of the translocations allow *ci* to manifest itself in heterozygous condition, and nine translocation suppress *ci*. There is no connection between the general properties of a given translocation and its effect on the degree of dominance of the normal allelomorph of *ci*. Among the ten translocations that

failed to suppress *ci*, some involved transfers of large and some of small sections of other chromosomes onto the fourth chromosome. Thus, the translocation of a large portion of the right limb of the third chromosome (breakage between *st* and *p*), on one hand, and the translocation of a minute section of the X-chromosome that is shorter than 0.6 unit on the other, both fail to suppress *ci*. The nine ineffective translocations are just as variable in size of the translocated sections as the ten effective ones.

In our cases the change in the degree of dominance of the wild-type allelomorph of *ci* depends neither on an alteration of the genic balance nor on a destruction of the genic material adjacent to the locus of breakage (see evidence presented below). No effect on the dominance of *ci* was observed in ten translocations not involving the fourth chromosome. Hence, two hypotheses may be formulated. First, mutations at the locus *ci* might have arisen during the process of translocation, and, second, the behavior of *ci* may be due to position effect.

The following experiments were carried out in order to test the nature of the alteration observed in the normal allelomorph of *ci*. Among the ten effective translocations studied, two translocations proved to be viable when homozygous. One of them (involving a transfer of a small piece of the left end of the X, breakage to the left of the viability gene) is rather poorly viable in homozygous condition, but the other (a II to IV translocation, breakage between *pr* and *c*) shows a normal viability. In case a recessive allelomorph of *ci* has arisen during translocation, these two translocations may be expected to show the characteristics of *ci* when homozygous. This is the more so since in the compound translocation/*ci* these translocations show the characteristics of *cubitus interruptus* to about the same degree as flies homozygous for *ci*. Nevertheless, flies homozygous for these translocations proved to be normal.

These experiments were extended by using flies heterozygous for two "effective" translocations. If recessive allelomorphs of *ci* were present in these translocations, such double heterozygotes should have shown *ci* in their phenotype. Eight such heterozygotes coming from the most effective translocations were studied, and all proved to be wild-type. Finally, most favorable conditions for the manifestation of the assumed recessive allelomorphs of *ci* were created. This was attained through the use

of Haplo-IV flies heterozygous for some of the "effective" translocations. In Haplo-IV the characteristics of *ci* may be exaggerated. Four effective translocations were tested in Haplo-IV condition, but all flies obtained were wild-type. We may conclude that no mutation at the *ci* locus arose during translocation. It is evident that not mutational changes at the *ci* locus, but the occurrence of the translocations themselves is responsible for the change in the degree of dominance of the wild-type allelomorph of *ci*.

It should be emphasized that no specific interaction between the gene *ci* and translocations themselves is observed. Translocations from all chromosomes (including the Y-chromosome) may produce position effects. It is very remarkable that among the translocations studied the number of "effective" ones (10) and ineffective ones (9) are approximately equal. This suggests that the locus of attachment of the transposed section to the fourth chromosome may be of a decisive significance for the production of the position effect. It is possible that an attachment of a chromosome fragment to one of the ends of the fourth chromosome (perhaps to the end where *ci* is located) produces the position effect, and the attachment to the opposite end does not. Various degrees of the weakening of the dominance of the wild-type allelomorph of *ci* are observed in different translocations. There is no connection between the effectiveness of a given translocated section and its origin from one or another of the chromosomes. The effectiveness probably depends upon the quality of the genes located close to the attachment point in the translocated section.

The behavior of *ci* in translocations suggests a difference between the reduction of dominance due to position effect and that due to transgenations. In case of position effect the result manifests itself only in compounds with the recessive allelomorph, but not in homozygous condition or in Haplo-IV. This indicates that the presence-absence theory, which considers all recessive genes as deficiencies of various sizes, is erroneous. In our case a difference is observed between the action of the recessive allelomorph of *ci* and that of the absence of *ci*. It is, of course, difficult to tell whether the effect of position is restricted to changes in dominance relations, or whether other properties of the genes, such as rate and direction of mutations, are also changed. Special experiments are needed to answer this question.

Most of our translocations are lethal when homozygous. Thus, alterations have taken place in the donor chromosomes (lethal effects) and in the recipient chromosome (change in the dominance of *ci*). The lethal effects are not necessarily due to position effects, since they might be produced also by destruction of the genes located near the loci of breakage. In one translocation, however, a lethal effect and a change in the dominance of the hairy gene (*h*) occurred in the donor chromosome simultaneously with the effect on *ci* in the recipient chromosome. The change in the dominance of the *h* gene in the donor is due to a position effect and not to a transgenation, since a heterozygous deficiency does not manifest any characteristics of hairy. The characteristics appear only in the presence of a recessive hairy gene (compound translocation/hairy). Thus, in this case we have a position effect both in the donor chromosome (*h*) and in the recipient chromosome (*ci*).

It is necessary to emphasize that in our cases the position effect may be proven because the genes *ci* and *h* are probably not hypomorphs in the sense of Muller (1932). Position effect in hypomorphs may be extremely difficult to distinguish from mutational changes.

The reduction of dominance results in the occurrence of a new hypomorphic recessive allelomorph that is not qualitatively different from the corresponding dominant. Many alterations of genes arising simultaneously with chromosome aberrations (translocations, deletions, inversions) which have so far been regarded as transgenations, may possibly be results of position effect.

Our data on position effect suggests that this phenomenon is generally rather wide-spread, and is of great importance for the manifestations of many genes. In the light of our data all cases in which the existence of position effect has not been previously convincingly proven become more convincing. The phenomenon of position effect opens a new page in the history of our knowledge of the structure of chromosomes. It suggests the existence of some intergenic connections. The position effect shows that although the chromosome structure is discontinuous (because it consists of genes) it is, owing to the intergenic connections, at the same time a continuum.

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RESEARCH ON PHYLOGENY OF SPECIES AND OF SINGLE CHARACTERS

(SIPPENPHYLOGENETIK UND MERKMALSPHYLOGENETIK)

THERE are few scientific branches in which the authors submit to as many misunderstandings as in phylogeny. If the authors write in different languages such misunderstandings are especially easy. In avoiding at least this one source of misunderstanding—the difference of language—it shall be tried to discuss shortly the aims of the author's "Phylogenie der Pflanzen" in connection with a report in another periodical.

Formerly the main aim of the phylogeneticists was in most cases undoubtedly the "genealogical tree." Such a phylogeny that aims at showing the connections of families, genera and species etc., in short, of "Sippen" (kinship) in a genealogical tree, has been called by the author "research on phylogeny of species" (= Sippenphylogenetik). This "research on phylogeny of species" is certainly a very important branch of scientific work. It is worth all advancement and has also been taken into consideration in the above mentioned book. *But this research on phylogeny of species is not the only phylogenetical science.* It must be considered that the research on phylogeny of species is a particularly difficult branch of phylogenetical research, and its results are subject to hard struggles. We never (except for mutations in genetical experiments) know directly the connections of species as we know the genealogical connections of human lines of descent and genealogical trees. We always conclude the phylogenetical connections of species only

according to the principle: "similar . . . therefore nearly related." It has frequently been emphasized that such a conclusion is often wrong and therefore can not be applied but with the greatest caution. Convergent evolution, parallel evolution, slow evolution, atavisms, etc., can as well produce similarities without near phylogenetical relationship.

But there are phylogenetical assertions which are entirely independent of these great difficulties of the "phylogeny of species." They are the assertions on the *"phylogeny of single characters"* (=*"Semophyletik or Merkmalsphylogenetik"*) that are dealt with in the first place in the "Phylogenie der Pflanzen." For explanation an example will be discussed, of which the facts are generally known. For a long time the character of the number of toes of horses has been treated "merkmalsphylogenetisch" (in the manner of research on phylogeny of single characters). Everybody is convinced that the one-toed foot of recent horses developed from the four-resp. five-toed foot of the horse ancestors. This "semophyletical" factum of variation of a single quality, namely the number of fully developed toes of the adult horse, is nowadays generally recognized in spite of the great difference in views about the "phylogeny of species" on the fossils, formerly as to-day.

Botanical phylogeny, too, knows such research on phylogeny of single characters. Only think of the "overtopping theory" (Uebergipfelungstheorie) by Potonié, *i.e.* the derivation of the pinnated fern-frond by overtopping of single joints ("Phylloide") from the fork-like geniculated (gegabelten) "leaf" of the ancestors—or the stelar theory by Jeffrey, *e.g.*, the derivation of the eustele from the protostele, the derivation of the anisogamy from the isogamy, and so on. Such derivations, *e.g.*, certainly took place parallel in different lines. Our assertions on the "phylogeny of single characters" are accordingly independent of the question of convergence or parallel development which is so hard to decide for the "phylogeny of species."

A few more words on a misunderstanding that occasionally turns up. The phylogeneticist of single characters does by no means maintain that the single characters developed at all isolated, independent of the "species-phylogenetical" connections. He does not do so any more than the cytologist says that a nucleus-division takes place isolated, independent of the rest of the ontogenetical events. It is only a technical simplification

if we consider at first isolated the phylogenetical transformation of a single character or the progress of nucleus-division.

The advantages of treating single characters separately are in the author's opinion, as indicated above, in the better reliability of our assertions. We are thus able to apply to phylogenies an important *instrument of exact research work: the number.* We are quite often able to assure our assertions on "phylogeny of single characters" by numerical treatment of the material ("statistic-phylogenetical method," *cf.* Zimmermann, 1931 and 1932). Just one example of general interest (Fig. 1). The fossil remains of the vasculiferous plants belong to the following types of propagation; the oldest forms (early Devon) are all (100 per cent.) isospore spore plants. In the upper Carboniferous the heterospore plants reach their maximum; *i.e.*, there are, beside a small number of seed plants and the considerably diminishing isospore forms, nearly 50 per cent. of heterospore plants present. To-day the seed plants are plainly dominating.

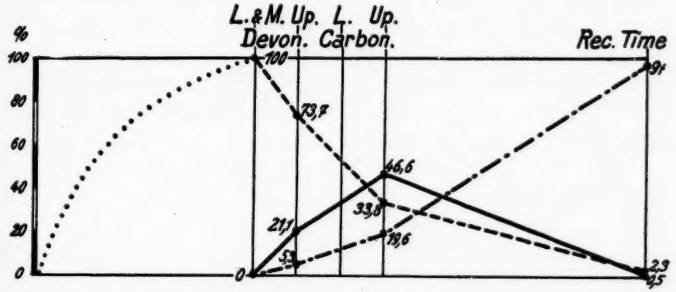

FIG. 1. Types of propagation in the past and present. ---- Isospory. —— Heterospory. . — Seed-Plants. The number gives the percentage of species with this type of propagation. (Zimmermann, 1932, Fig. 4.)

The isospory has accordingly been replaced by heterospory and that again by the propagation through seeds. Such statistic treatment of "merkmalsphylogenetische" problems shows that Hofmeister's old supposition of a transformation: isospory—heterospory—seed-propagation is undoubtedly right in a phylogenetical sense, though it has lately been attacked.

The difference between research on "phylogeny of species" and research on "phylogeny of single characters" is very clear in the attitude towards the question of *monophyletical or polyphyletical evolution.* Nägeli, Hanstein, Reinke, and many other

botanical authorities hold the opinion that "the species" arose "polyphyletically" by numerous single acts of spontaneous generation and developed in parallel lines to their present state. Lotsy, the author of the well known "Stammesgeschichte der Pflanzen," holds the opinion that such primitive forms were generically different from the first. Hayata, too, takes up this idea in his much discussed "Dynamic System."

The usual monophyletical orientated research on "phylogeny of species" is of course not combinable with such extremely polyphyletical views (that in the author's opinion are not at all proved). Assertions on phylogeny of single characters are entirely independent of such contrasts about "monophyletical" or "polyphyletical" relationships. Even in case there were no real genealogical relations existing in the sense of Reinke, Nägeli, and Hanstein, or in case these relationships were most different from our present suppositions, our cited assertions on phylogeny of single characters would still remain.

It must not be forgotten that the *causal-phylogenetical problems* which are usually discussed under the catch-word of *Darwinism and Lamarckism* equally do not refer to the more statistically orientated research on "phylogeny of species," but treats questions of a rather kinetically and dynamically orientated research on "phylogeny of single characters."

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